Guidelines for the assessment and treatment of Clozapine Induced Constipation

Scope

This guideline is intended to support the appropriate assessment of patients prescribed clozapine to enable the early identification and treatment of clozapine induced constipation. It is relevant to healthcare professionals across NHS Greater Glasgow & Clyde involved in the care of people prescribed clozapine.

Background

Clozapine is a second generation antipsychotic licensed for treatment resistant schizophrenia, for use in patients intolerant of other antipsychotics and for the treatment of psychosis in Parkinson’s disease. Clozapine has a range of potentially troublesome side effects, some of which can have significant impacts on patients’ physical health. National guidelines to support improved physical health monitoring of patients prescribed clozapine were published by the Scottish Government in 2013 (1).

Constipation is a very common side effect of clozapine. It is estimated that up to 60% of patients who are prescribed clozapine experience constipation (2). Although rare, death from complications arising from constipation is estimated at more than three times the rate of death from agranulocytosis (2). Severe complications associated with clozapine induced constipation include intestinal obstruction, faecal impaction and paralytic ileus. Despite this however, unlike for blood dyscrasias, there are no mandatory requirements to monitor patients for and actively treat clozapine induced constipation.

Many services have begun to introduce more structured processes for physical health monitoring but there is a need for a systematic, frequent assessment to identify patients experiencing clozapine induced constipation and then implement effective treatment.

Risk factors for constipation are:

- Recent initiation of clozapine (greatest risk is during the first four months of treatment, but the risk persists)
- High dose or plasma clozapine level
- Intercurrent illness
- History of bowel surgery
- Concurrent use of other drugs known to cause constipation (opioids, drugs with anticholinergic properties. This includes most of the treatments for clozapine-induced hypersalivation e.g. hyoscine hydrobromide).
- Lifestyle issues e.g. poor diet and lack of exercise.
- Learning disability
- Old age
- Obesity

This guideline provides advice to services in NHS GG&C to support systematic assessment and treatment of clozapine induced constipation.

Approved: May 2020
Review date: May 2023
Assessment

Patients prescribed clozapine are regularly in contact with NHS services in order to undergo mandatory full blood count testing. That frequent contact presents an opportunity to systematically assess patients for common serious side effects. There are two distinct phases to clozapine treatment, a titration/stabilisation phase and a maintenance phase. Assessment of clozapine induced constipation is appropriate in both phases. There must be a systematic, documented and reliable process of assessment throughout clozapine treatment.

It should be noted that clozapine has a greater potential for gastro-intestinal side effects compared with other antimuscarinic agents, possibly because of its anti-serotonergic properties. This may lead to slower colon transit, reduced gastro-colonic reflexes, increased colonic compliance and perhaps reduced intestinal sensitivity to distension. This means that patients may not complain about constipation and therefore should be asked regularly about bowel habit.

The risk of developing clozapine induced constipation should be clearly identified within care plans.

1. Titration/stabilisation phase

   • During the work up for clozapine treatment, patients should be assessed for risk factors for constipation including previous history, concurrent treatments likely to induce constipation and lifestyle factors.
   • Active bowel monitoring should occur throughout this phase at each clinically appropriate contact (Appendix 1 and 2). The use of daily bowel charts should be considered. Tools like the Bristol Stool Chart (see clozapine care plan in GG&C Clozapine Standards) should be used to help identify constipation.
   • Any change in bowel habit should be immediately reported to the multi-disciplinary team and constipation actively treated (Appendix 3).
   • Educate patients and carers about the risk of constipation. Consider providing the Choice and Medication Clozapine and Constipation Handy Fact Sheet (http://www.choiceandmedication.org/nhs24/ )


Patients with no history of constipation

   • Patients should be assessed for constipation at every visit for their full blood count (Appendix 1). Tools like the Bristol Stool Chart should be used to help identify constipation.
   • Any patient reporting changes in their bowel habit, abdominal pain or having less than 3 bowel movements per week must be immediately referred for a thorough medical assessment including an abdominal examination if necessary (Appendix 3).
   • Any patient with a high clozapine plasma level should be immediately examined for constipation.

Patients undergoing treatment for clozapine induced constipation

Approved: May 2020
Review date: May 2023
Any patient who is already receiving laxative treatment for clozapine induced constipation who continues to report problems should be referred for further medical assessment including an abdominal examination if necessary.

Any patient with a high clozapine plasma level should be immediately assessed for constipation.

*Note: for the CMHTs referral would be to the patient’s GP or if symptoms are severe to A&E. For patients in hospital contact the duty doctor. The patient’s Responsible Medical Officer (RMO) must always be informed.

**Recording bowel function**

A standardised approach to recording bowel function should be adopted and include numerical values for Bristol Stool Chart type and frequency. For example:

BSC (Bristol Stool Chart) - 4

BM (Bowel motion) - 2/7

**Treatment**

When clozapine induced constipation has been identified the following steps are recommended:

- Recommend changes in lifestyle, diet and fluid intake
- Consider reducing the clozapine dose
- Stop or reduce medications that can cause constipation
- Flowcharts in appendices 2 and 3 give guidance on the recommended management of clozapine induced constipation.
- Review compliance regularly and if necessary prescribe more palatable options e.g. docusate. Patients frequently have issues complying with laxative treatment as they may be quite unpalatable.
- If severe symptoms emerge e.g. abdominal pain, distension, vomiting, overflow diarrhoea, absent bowel sounds, acute abdomen, feculent vomitus or symptoms of sepsis, take the following steps
  - Stop clozapine and all other anti-muscarinic medicines
  - Refer for emergency medical treatment
  - Assess for bowel obstruction
- Patients presenting with diarrhoea may be constipated with main symptom presenting as overflow and that should be excluded before any treatment is considered.

For patients who cannot reliably identify bowel problems, the use of preventative laxative treatment throughout clozapine treatment may be appropriate. It should be noted that prolonged use of stimulant laxatives may lead to degenerative changes in colonic muscles and nerves.
References

2. Fact Sheet; Constipation. ZTAS December 2013
Appendix 1- Clozapine induced constipation monitoring

How many bowel movements (BM) are you having per week?

Record on EMIS:

- e.g. 3 x BM/week

Could you rate your bowel movements using the Bristol Stool Chart (BSC)?

Record on EMIS:

- e.g. BSC 3-4

BSC 1-2?

- Or
- <3 BM/week?
- Or
- Abdominal pain?

Follow flowchart in appendix 3

Yes

In community patients should be referred to their GP unless symptoms are severe
RMO should be informed

No

BSC 7 preceded by period of severe constipation?

Yes

Refer to duty doctor – with a view to sending for emergency medical treatment

No

No further action needed

Approved: May 2020
Review date: May 2023
Appendix 2- When commencing clozapine

- Counsel patient/carer on gastrointestinal side effects and risks of clozapine
- Provide lifestyle advice on dietary intake, fluid intake and regular exercise
- Review concomitant medication that can cause constipation if appropriate
- Consider the addition of an appropriate osmotic laxative. E.g. Macrogol oral powder (Laxido) 1 – 3 sachets daily or lactulose 15ml twice daily.
  - Adequate fluid intake (2-3 litres daily) is essential but caffeine containing drinks should be avoided.
- Actively screen and monitor for symptoms and complications of constipation
Appendix 3- Clozapine induced constipation treatment

Recommend changes in lifestyle, diet & fluid intake. Provide NHS inform leaflet. Check compliance with prescribed laxatives.

Consider reducing the clozapine dose.

Stop or decrease medications that can cause constipation.

Consider the addition of an appropriate osmotic laxative. E.g. Macrogol oral powder (Laxido) 1 – 3 sachets daily or lactulose 15ml twice daily.

Adequate fluid intake (2-3 litres daily) is essential but caffeine containing drinks should be avoided.

Add a **stimulant laxative**

If ineffective after several days, add senna 2-4 tablets at night (Short-term only)

Docusate with both softening and stimulant properties may be an alternative.

Softening or stimulating enemas would also be alternative options.

Stop clozapine and other antimuscarinic agents.

Refer for emergency medical treatment.

If intestinal obstruction is excluded

Combinations of laxatives are often required

Consider patient tolerability and preference

Prolonged use of stimulant laxatives may lead to degenerative changes in colonic muscles and nerves

If severe symptoms emerge e.g. abdominal pain, distension, vomiting, overflow diarrhoea, absent bowel sounds, acute abdomen, feculent vomitus or symptoms of sepsis or intestinal obstruction is suspected