Sheffield Children's NHS
NHS Foundation Trust

Investigation, Management and Treatment of Diarrhoea (for patients receiving chemotherapy or radiotherapy)

Reference:	CG904
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Approved by RRGM:	11th April 2023
Approved by D&TC:	16th December 2022
Review Due:	April 2028

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Intended Audience

This document contains information and clinical guidelines for management of children attending the Oncology and Haematology department. It is to be used by staff within the Trust whenever they are caring for these children either in hospital or at home.

Purpose

To provide guidance on the investigation, management and treatment of diarrhoea in haematology and oncology patients.

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Diarrhoea

1. Introduction

Diarrhoea can be a debilitating, and potentially serious, consequence of chemotherapy or abdominal radiotherapy. Urgent investigation of the underlying cause, to exclude infection and ascertain the extent of damage to the GI tract, is essential.

Diarrhoea, even without fever, can be a symptom of severe infection in the neutropenic patient. See The Haematology & Oncology Unit guidelines, Section 6: Infection, 854 Febrile Neutropenia – Investigation and Initial Treatment (H&O/06/854).

2. Potential Causes

These are divided into non-infective and infective causes.

Non Infective

Cause	Features
Mucositis secondary to chemotherapy	Low volume, often also nausea and anorexia. Severity depends on type of chemotherapy. High dose methotrexate is particularly high risk.
Medication	e.g. Irinotecan, Cisplatin, Fludarabine, some antibiotics, laxatives, metoclopramide
Constipation with overflow	Extensive faecal loading may be seen on plain abdominal X ray
Radiation enteritis	May occur during abdominal radiotherapy, particularly to pelvis. Can also occur as late complication following radiotherapy

Infective

Cause	Features
Viruses	Adenovirus, Rotavirus, HSV, CMV, Parvovirus. (CMV enteritis is often associated with bloody diarrhoea, but is rare in non-transplant patients.) See Haematology/Oncology guidelines Section 6, 857 Management of suspected viral infection (H&O/06/857)
Fungi	Fungal overgrowth can lead to watery diarrhoea. See Haematology/Oncology guidelines section 6, 856 management of suspected fungal infection (H&O/06/856)
Parasites	Cryptosporidium, Giardia lambia, entamoeba histolytica can all cause diarrhoea, but not commonly
Clostridium difficile	Toxin related symptoms usually associated with antibiotic treatment
Bacterial	Bacterial causes responsible for diarrhoea may be a symptom of onset of septic shock- see introduction above.

3. Investigation

Document volume, consistency, colour and presence of mucous or blood in stool.

Stool should be sent for microscopy, bacterial cultures and virology - These should be tested repeatedly in patients with persistent symptoms.

A plain abdominal X-ray may help in differentiating constipation with overflow

If symptoms recur or persist for 7 days in the absence of a positive culture, consult gastro-enterology team with a view to upper and lower GI endoscopy.

4. Management

General principles

Isolation and hand washing (by patient, carers and staff) and dietary restrictions until the aetiology is known are important preventative measures in spreading infection.

Enteral feeding will exacerbate diarrhoea related to mucositis because of fat and carbohydrate malabsorption. However, as luminal nutrients are needed for gut repair, it is desirable to continue enteral feeds if possible. In cases of rotaviral infection feeding should be stopped during the acute phase of the illness particularly but re-instated as soon as possible.

Supportive care

Pay attention to fluid balance, acid base balance and electrolyte levels. Replace fluids with maintenance fluid using an isotonic solution such as sodium chloride 0.9% with or without glucose 5% + % replacement for losses (see SC(NHS)FT Medical Guidelines for Paediatric Medicine, 1.12, Diarrhoea & Vomiting in Children Reg ID No 1088).

Add electrolytes (See The Haematology & Oncology Unit guidelines, Section 5: Chemotherapy, 1498 Correction of Electrolyte Disturbance (H&O/05/1498)) as required.

If there are signs of shock due to >10% dehydration

- Inform the SpR or consultant immediately.
- Oxygen should be administered to maintain adequate oxygen saturation, if necessary.
- Give a fluid bolus – 20mls/kg of 0.9% sodium chloride IV and reassess.
- Inform ICU using the "Early warning alert" process as soon as the first bolus has been given.
- Review the patient with a haematology/oncology registrar grade or above and discuss subsequent management with ICU staff as appropriate.
- Monitor vital signs and urine output closely (half hourly to hourly depending on patient status). Urinary catheterisation may be necessary if no urine output, despite improvement in haemodynamic status.

Consider whether feeds need to be reduced or stopped. PN should be started for severe mucositis with an anticipated duration of more than 7 days, or in the malnourished child. See The Haematology & Oncology Unit Guidelines, Section 5: Chemotherapy, 902 Mouth Care (H&O/05/902) for details of appropriate anti-infective prophylaxis and pain relief for severe mucositis.

Stop any exacerbating drugs if possible.

5. Treatment

Treat with loperamide only if cultures are negative and there is no blood in the faeces.

LOPERAMIDE		
Age:1 month- 11 months	1-11 years	12-17 years
100-200microgram/kg usually twice daily. *(Frequency can be increased if required to a max 2mg/kg/day in divided doses)*	**100-200microgram/kg (max 2mg) 3-4 times a day** **frequency can be increased if required up to 1.25mg/kg/day in divided doses.** *(Max 16mg/day)*	**2-4mg** **usually 2-4 times a day** *(Frequency can be increased if required to a max 16mg/day in divided doses)*

If the diarrhoea is still not controlled on maximum loperamide dose of 16 mg/day discuss with consultant regarding further management

Clostridium difficile can cause toxin related symptoms. Choice of antibiotic treatment depends on severity of symptoms and the patients risk of severe disease. Patients with mild symptoms and a relatively low risk of severe disease should be treated with oral metronidazole for 10 days. All other patients should receive oral vancomycin for 10 days. See BNFc for doses. Intravenous metronidazole should only be used if the patient is nil by mouth. Intravenous vancomycin is ineffective against GI infection with *C.difficile*. Discuss with microbiology if cases of recurrent infection or symptoms unresponsive to treatment.

Virus specific treatment should be considered in patients with enteritis due to Adenovirus, CMV, HSV and possibly Rotavirus. This should be the decision of the consultant or Specialist Registrar. See The Haematology & Oncology Unit Guidelines, Section 6: Infection, 857 Management of Suspected Viral Infection (H&O/06/857)

The gastroenterology team should be consulted for patients with intractable chronic diarrhoea with a view to endoscopy and gut biopsies. There is limited evidence for the use of octreotide for the management of refractory chemotherapy induced diarrhoea. See Appendix for doses.

Diarrhoea

Irinotecan induced diarrhoea

Diarrhoea is a known side effect of irinotecan, this can be acute onset (immediately after drug administration) or delayed (24 hours after infusion).

Diarrhoea occurring with acute cholinergic syndrome starting immediately after, or during administration of irinotecan can be treated with iv/sc atropine 20micrograms/kg (max 250 micrograms).

Patients should be made aware of the risk of delayed diarrhoea occurring more than 24 hours after the administration of irinotecan and at any time before the next cycle.

Cefixime at a dose of 8mg/kg (max 400mg) once daily can be given to prevent diarrhoea associated with irinotecan. Loperamide should also be given to the patient to start with the first loose stool.

6. References:

Paediatric Formulary Committee. British National Formulary for Children (online) London: BMJ Group, Pharmaceutical Press, and RCPCH Publications www.medicinescomplete.com [Accessed 18/08/2022]

Lexicomp Pediatric and Neonatal Dosage Handbook (online). Available at https://online.lexi.com [Accessed 18/08/2022]

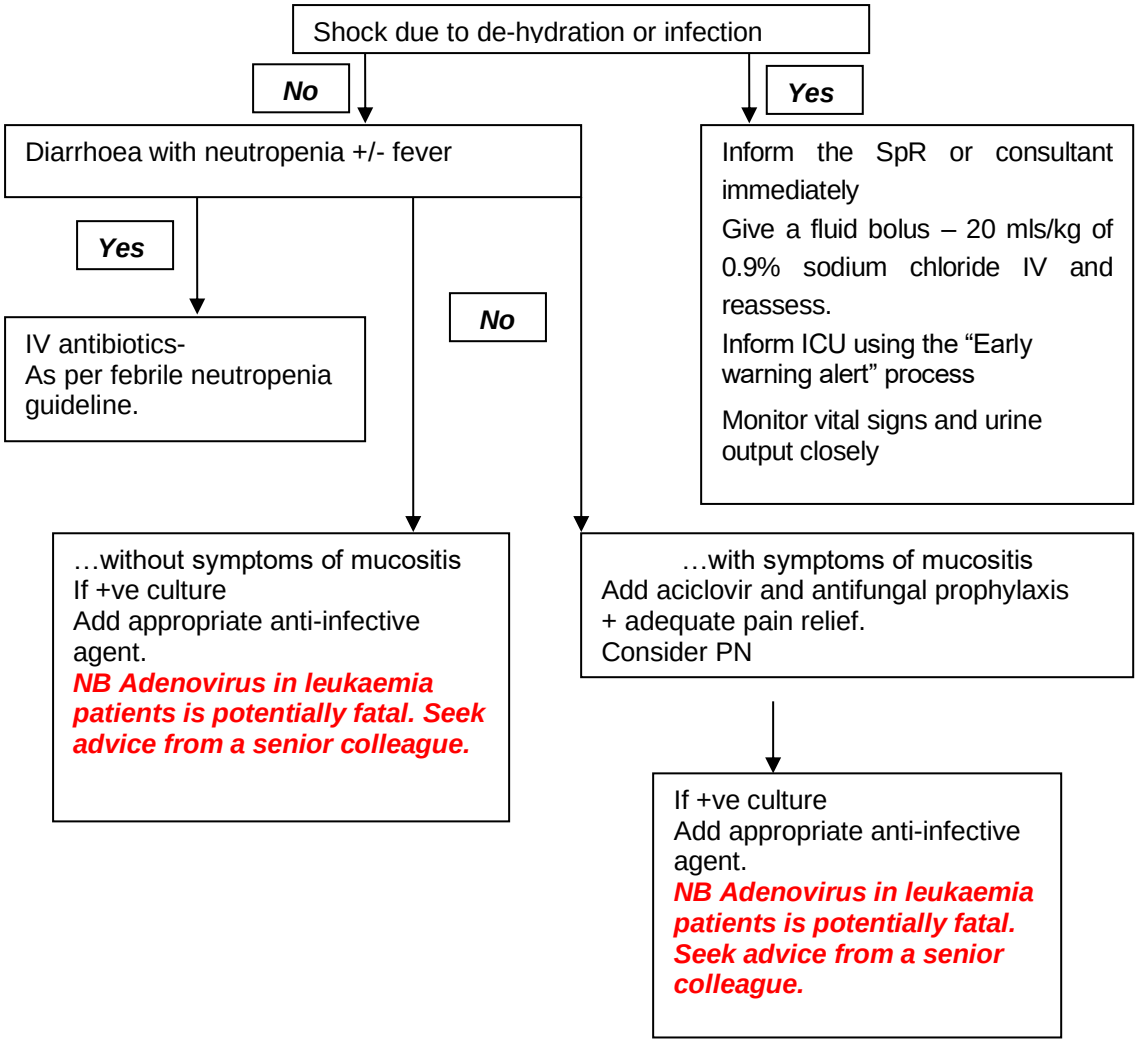
FaR-RMS protocol, V2.0b, Dec 2021. University of Birmingham, CRCTU

Medical Staff guidelines Sheffield Childrens (NHS) Foundation Trust

Diarrhoea

Flow diagram

See also Haematopoetic stem cell transplant SOPs - management of diarrhoea (HSCT/048) and management of viral infections (HSCT/039).



Diarrhoea

Appendix I

<table>
<tr><th colspan="2">Octreotide</th></tr>
<tr><td>Presentation</td><td>50micrograms/ml Injection, 100micrograms/ml injection, 500micrograms/ml Injection</td></tr>
<tr><td>Indications & Dosage</td><td>Refractory diarrhoea:
Subcutaneous dose: 1-10micrograms/kg every 8 to 12 hours. Start at the low end of the range and titrate to effect.

Continuous IV infusion: To be used if intermittent s/c dosing is not effective. Start at 1microgram/kg/hour (usually max 50microgram/hour) continuous IV infusion, increasing gradually every 48 hours until diarrhoea controlled. Octreotide infusion should be withdrawn slowly . Halve the rate very 6-12 hours.

Gastro consultants may recommend 1-5microgram/kg/hour for secretory diarrhoea. See SCHFT Intravenous drug administration guide for octreotide</td></tr>
<tr><td>Side-effects</td><td>Most commonly anorexia, nausea, vomiting, abdominal pain. Hyperglycaemia, hypoglycaemia, hypothyroidism, dizziness, headache, pancreatitis, inhibition of gall bladder motility, bile acid secretion and bile flow. Rises in liver enzymes. Isolated reports of abrupt withdrawal have been associated with biliary colic and pancreatitis. Ileus if continued once diarrhoea settled. Pain at the site of injection is common</td></tr>
<tr><td>Reconstitution & Dilution</td><td><u>For IV administration</u>:
Each vial size should be diluted with sodium chloride 0.9% to not less than 1 to 1 and not more than 1 to 9 by volume, ie:
<table>
<tr><th>Vial size</th><th>Dilute to a final concentration of between</th></tr>
<tr><td>50micrograms/ml</td><td>5 micrograms/ml – 25 micrograms/ml</td></tr>
<tr><td>100micrograms/ml</td><td>10 micrograms/ml – 50micrograms/ml</td></tr>
<tr><td>500micrograms/ml</td><td>50 micrograms/ml – 250micrograms/ml</td></tr>
</table>
Stable for 8 hours</td></tr>
<tr><td>IV Bolus</td><td>Not recommended for treatment of diarrhoea</td></tr>
<tr><td></td><td></td></tr>
<tr><td>Continuous Infusion</td><td>See above for reconstitution, prescribe on the continuous IV drug infusions section of the drug chart.</td></tr>
<tr><td>SC Administration</td><td>Warm to room temperature before administration. Administer dose without dilution.</td></tr>
<tr><td>Maximum Concentration</td><td>See above</td></tr>
<tr><td>Cautions related to Administration</td><td>Monitor blood glucose.</td></tr>
<tr><td>Comments</td><td>Dilution with glucose is not recommended
Compatible to Y-site with PN</td></tr>
<tr><td>References</td><td>1. Paediatric Formulary Committee. BNF for Children (online). London: BMJ group, Pharmaceutical Press & RCPCH publications. www.medicinescomplete.com [accessed 08/2022]
2. Evelina London paediatric formulary (via app) [accessed 08/2022]
3. Lexicomp Pediatric and Neonatal Dosage Handbook (online). Available at https://online.lexi.com [accessed 08/2022]
4. Ranbaxy (UK) Ltd (13-Oct-2021). Octreotide 50microgram/ml, 100microgram/ml and 500microgram/ml solution for injection. Summary of product characteristics.</td></tr>
</table>