THE MANAGEMENT OF ACUTE DIARRHOEA IN A HEALTHY ADULT POPULATION DEPLOYING ON MILITARY OPERATIONS

S Bourne[1], C Petrie[2]

[1]Consultant Physician, Southampton University Hospitals NHS Trust. [2]ST1 Medicine. MDHU Peterborough.

Abstract

Acute diarrhoea is consistently the number one presentation to secondary care facilities on UK military operational deployments. It can result in potentially life threatening consequences as seen on Operation Herrick in 2002, where a Norwalk-like virus caused 3 cases of meningo-encephalitis. Due to the circumstances of communal accommodation, ablutions and dining facilities, even mild cases are admitted at role 2, and personnel are not discharged until fully recovered in order to prevent potential outbreaks. This literature review examines the management of acute diarrhoea in healthy adults relating to UK military operations, and presents a management algorithm suitable for any theatre. The importance of the initial assessment is highlighted and allows the severity of the condition to be assessed using three key parameters. We recommend the selective use of stool culturing for severe cases and outbreaks. The use of oral re-hydration solutions vs. intravenous fluids, and the indication for the safe use of anti motility agents and antibiotics for diarrhoea are discussed. Where pathogens are yielded local sensitivities should guide the choice of treatment. Salmonella spp and Shiga toxin-producing E.coli (STEC) should receive supportive care only.

Introduction

Acute diarrhoea is consistently the number one presentation to secondary care facilities on UK military operational deployments. It can result in potentially life threatening consequences as seen on Operation Herrick in 2002, where a Norwalk-like virus caused 3 cases of meningo-encephalitis [1]. Due to the circumstances of communal accommodation, ablutions and dining facilities even mild cases are admitted at role 2, and personnel are not discharged until fully recovered in order to prevent potential outbreaks.

Background

Diarrhoea is one of the most common conditions to present to primary and secondary care. It ranks second only to upper respiratory tract infection as the most common affliction of individuals throughout the world [2]. It is a disease with both clinical and public health relevance with a worldwide incidence of 0.5-2 cases per person per year [1]. In the United States (US) the incidence is 1.4 overall and is highest in children aged 6-11 months at 4.8 episodes per child per year [3, 4]. It accounts for 20% of GP consultations in the UK for children under the age of 5yrs. There are an estimated 20 million cases of travellers' diarrhoea annually affecting up to 50% of travellers to developing countries [5].

It is a major cause of morbidity and mortality and is in the top 5 causes of death worldwide, causing 2 million deaths annually and responsible in the US for 8 million doctors visits and 250-900,000 hospital visits every year [6].

The majority of studies concentrate on acute diarrhoea in children, or within specific pathologies, and relatively few address the problem in the well adult population and hence there is variability in practice between health care providers [7]. This literature review concentrates on the management of acute diarrhoea in the healthy adult and encompasses initial assessment, when to culture stool, the use of oral rehydration therapy (ORT), intravenous (IV) fluids, anti-motility agents, and finally antibiotic treatment.

Corresponding Author: Lt Col Simon Bourne MRCP(UK), MP 810 South Academic Block, Southampton General Hospital, Tremona Road, Southampton, SO16 6YD
Mobile: 07976 395850
Email: scbourne@msn.com

Methods

A literature review of Medline and pub med papers with the keywords diarrhoea and acute diarrhoea was used to search the literature from the year 1996 onwards. Studies and reviews were then assessed according to relevance and quality of research.

Definition

The common consensus of the definition of acute diarrhoea is 3 or more episodes of loose or watery stool within 24 hours, and lasting no more than 14 days. One or more episodes of bloody stool is also widely accepted [3].

Initial Assessment

The importance of the initial assessment of the patient cannot be underestimated and allows for a more evidence based and cost-effective approach to management. The initial assessment requires a detailed history of the diarrhoea, and a physical examination to determine the level of dehydration, and to exclude other pathology.

Stool frequency and type (according to the Bristol Stool Chart - Table 1), vomiting and abdominal pain should be included within the history [8]. Other important epidemiological factors including time of onset, travel, dietary intake, affected contacts and any medication used are also recorded. The Infectious Disease Society of America (IDSA) guidance uses a comprehensive combination of all the above, plus epidemiological characteristics and stool microscopy [9]. Unfortunately the predictive value for specific pathogens based on the presence or absence of blood, mucous, abdominal pain, travel history and epidemiological variables has been shown to be low, and they are more useful as a tool to guide the use of intravenous fluids, faecal testing and antibiotic therapy [7].

TYPE 1	Separate hard lumps like nuts (hard to pass)
TYPE 2	Sausage shaped but lumpy
TYPE 3	Sausage shape with cracks on the surface
TYPE 4	Sausage/snake smooth and soft
TYPE 5	Soft blobs with clear cut edges
TYPE 6	Fluffy pieces with ragged edges, a mushy stool
TYPE 7	Watery, no solid pieces entirely liquid

Table 1. The Bristol stool chart form scale adapted from [8].

Significant diarrhoeal illness is predicted by the presence of pyrexia, bloody stools or copious diarrhoea (there is no consensus of opinion to define this, but for the purpose of this paper is defined as more than 6 stools in 24hrs). These three simple parameters can be used as an indication for stool culture and will be discussed in more detail.

Assessment of hydration status should involve a detailed examination of pulse, skin turgor, jugular venous pulse, capillary re-fill time and mucous membranes. The assessment of dehydration can then guide re-hydration by classifying it as mild, moderate or severe (Table 2) [10].

The bacterial pathogens Campylobacter, Salmonella and Shigella are the top 3 causes of bacterial gastroenteritis worldwide. In the UK in recent years Campylobacter has increased in incidence at a higher rate than other pathogens [11].

In the UK and on operations we can routinely culture Campylobacter, Salmonella, Shigella and E.Coli. A positive culture is useful to aid treatment; however when acute diarrhoea typically lasts 1-3 days, and 50% last less than 24 hours, then in most cases the illness will have resolved before culture results become available. If we consider that stool culture yield has persistently been shown to be only 1.5-2.9%, and in turn cost $952-1200 per positive test, it is clear that it is only cost effective in certain circumstances [2, 7]. The presence of fever, bloody, and severe diarrhoea are indicators of severe illness. It is advisable therefore that in these cases cultures are taken as soon as possible.

Faecal lactoferrin screening is a test which may aid identification of inflammatory diarrhoea in equivocal cases. Lactoferrin is a breakdown product of polymorphs detected by latex agglutination. This is a simple and quick test and a positive result has some predictive value and may predict culture of Campylobacter, Salmonella and Shigella [2, 4]. However the sensitivities and specificities vary widely, so it is not generally used. It may however be a test more useful for its negative predictive value.

Parameter	**Mild**	**Moderate**	**Severe**
General State	Alert + Active	Weak, lethargic, but able to sit + walk	Inactive, unable to sit/walk
Ability to perform daily activity	Able to perform	Some difficulty	Unable to perform
Thirst	Not increased	↑	↑↑
Pulse Rate	N	↑PR	↑PR
Blood Pressure	N	↓by 10-20mmHg	↓by >20mmHg
Postural Hypotension	None	Occasional	Often
JVP	N	N/Flat	↓JVP
Mucous Membranes	N	Dry	Severely dry
Skin Turgor	N	N	↓
Eyes	Not sunken	Minimally sunken	Sunken

Table 2. Assessment of dehydration, modified from [4].

Manatsathit et al recommend abdominal and PR examination for every case to rule out alternative pathology, and confirm stool character respectively, this should not be necessary for the previously fit adult, and can be achieved by examining stool if required [10].

When to Culture?

Acute diarrhoea is caused by the pathogen listed in Table 3.

Viruses are responsible for 30-40% of cases of acute diarrhoea; those relevant to the healthy adult population are sporadic cases of rotavirus, adenovirus, astrovirus and calcivirus. Outbreaks commonly involve norovirus (a calcivirus previously known as Norwalk-like virus), the incidence of which is increasing annually [9].

Other circumstances relevant to the healthy adult are those of a suspected outbreak where it is recommended that routine testing extends to include norovirus. This is particularly prudent to the military deployment where outbreaks of the virus have been documented; however facilities in this situation do not extend to viral PCR as highlighted by the severe cases in Afghanistan in 2002. We therefore rely on quick access to laboratories in the UK to help with the identification of pathogens in such outbreaks [1]. There is an argument however that viral culturing is unnecessary as knowing the identity does not alter the management which is infection control and supportive therapy.

Viruses	**Bacteria**	**Protozoa**	**Helminths**
Rotavirus	*Vibrio spp*	*Giardia intestinalis*	*Strongyloides stercoralis*
Adenovirus	*Aeromonas*	*Cryptosporidium parvum*	*Schistosoma spp*
Calcivirus	*E.Coli spp*	*Microsporidia*	
Astrovirus	*Shigella spp*	*Isospora belli*	
Cytomegalovirus	*Salmonella spp*	*Cyclospora cayetanensis*	
	Campylobacter spp	*Entamoeba histolytica*	
	Yersinia enteroclitica	*Balantidium coli*	
	Clostridium difficile		
	Plesiomonas shigelloides		

Table 3. Enteropathogens adapted from [4].

In cases of persistent diarrhoea (>7 days), especially those related to travel, stool testing should extend to examination for ova, cysts and parasites to consider giardia or amoeba.

Re-hydration

All patients with acute diarrhoea will have an element of dehydration. There is strong evidence for the initiation of re-hydration, and it is the cornerstone of management [7].

The argument about whether this is achieved via oral re-hydration solutions (ORS) or via intravenous (IV) replacement is more complex. Adults are better at compensating for dehydration than children as they have a larger fluid reserve and therefore their clinical signs are less obvious. As mentioned in the initial assessment, only one set of guidelines specifically set parameters for the degree of dehydration in adults, setting parameters for mild, moderate and severe [10]. In terms of oral versus IV as the route, it is recommended to use the oral approach for 'mild' dehydration or more simply wherever oral intake is tolerated. The IDSA guidelines suggest the oral route is safer and less costly. The oral route is also safer in terms of physiologically regulating volume of fluids and electrolytes, the quantity guided using thirst and urine output. Where IV fluids are necessary electrolyte monitoring is essential.

There has been some considerable debate to which oral fluid to give, and it has been shown that the use of ORS improves mortality in childhood diarrhoea especially in under-developed countries. There are conflicting guidelines on the use of ORS in adults. The IDSA and Manatsathit et al promote the use of the WHO recommended formula for all patients but the evidence for this is based on those patients with a diagnosis of cholera. Nathan et al specify that adults should be encouraged to drink fluids and eat salt rich foods and Wingate et al state otherwise healthy adults do not require ORS and there is no evidence that the formulations relieve or shorten the duration of the diarrhoea illness [4, 12].

None of the literature reviewed evaluated whether ORS or IV fluids made patients subjectively feel any better.

Anti-diarrhoeal Medications

The most commonly recommended anti-diarrhoeal medication for adults is Loperamide which is an antiperistaltic and antisecretory agent. This has been shown to reduce the volume and frequency of stools, shorten duration of symptoms and demonstrated good efficacy and safety in randomised, controlled trials by the American Food and Drug Administration. The majority of literature specifies its use in cases of mild severity, and it is recommended for use as self-medication in mild acute diarrhoea. It should not be used in 'inflammatory diarrhoea' defined as bloody diarrhoea, severely unwell or febrile patients. The intestinal stasis is thought to enhance the tissue invasion of bacterial pathogens and there is evidence that using it prolongs fever in Shigellosis [4, 10, 12].

Other motility agents are described in the literature such as adsorbents but these have insufficient clinical data to support their use. Bismuth subsalicylate has been found to be effective in some trials, but was not as effective in comparison to loperamide, and has the unfortunate side effect of causing blackening of the tongue and stool [4].

Antibiotics

Appropriate antibiotics can be effective but there are increasing problems with antibiotic resistance as well as side effects, harmful eradication of normal flora and even controversial evidence of the induction of Shiga-toxin production. Consideration of antimicrobial treatment must therefore be carefully considered [4].

The quinolone ciprofloxacin has historically been the treatment of choice but dramatic increases in resistance has been seen in Campylobacter infections since the 1990s and it has also been shown to worsen infections due to eradication of competing normal flora. Erythromycin is the drug of choice in these cases and has been shown to have an impact on duration of symptoms and reducing pathogen carriage when given early (within the first 4 days of onset).

Salmonella species have similarly seen an increase in their resistance to quinolones and antibiotics have been shown to be ineffective, associated with prolonged carriage and even relapse. To this end antibiotic treatment for Salmonella is only recommended in certain situations that do not relate to the otherwise healthy adult [4, 10].

There is good evidence from randomised, controlled trials however that treatment of Shigella with quinolones has good efficacy and reduces both duration of fever and length of symptoms by over 2 days and reduces organism shedding [7].

Antibiotic therapy for Shiga toxin-producing E.coli (STEC) is not recommended due to the increased rate of haemolytic uraemic syndrome (HUS) seen in treated patients and supportive care only is the ideal strategy.

Considering the above it is clear that despite it being more clinically practical to consider guidelines for empirical treatment they are difficult to follow and contradictory. Mainly because even the advice regarding specific antimicrobials for isolated organisms is complex and we know that pathogens are rarely yielded from culture, take 48 hours to grow and the value of predicting organisms from history and examination is low.

Looking at the Empirical treatment advice there are two situations where recommendations are clear and consistent. The first is the empirical treatment of travellers' diarrhoea which has demonstrated good response to antibiotic treatment in clinical trials since the 1980s and repeatedly done so in double-blind placebo-controlled trials even with a single dose of Ciprofloxacin reducing duration from 3-5 to <1-2 days [4, 5, 7, 10, 12]. This is interesting when as many as 25% of travellers' diarrhoea cases have been shown to be due to invasive pathogens including Salmonella and Campylobacter [4, 5, 7, 10, 12].

The second circumstance described is that of using Metronidazole for persistent diarrhoea lasting >7-10 days where the protozoal pathogen Giardia is the most likely suspect especially when the stool culture is negative and the illness is associated with history of travel or water exposure.

Other empirical treatment advice for healthy adults centres on giving ciprofloxacin to the patient with bloody and febrile diarrhoeal illness and may reduce the duration of illness and carriage of pathogen. This is again contradictory when it is considered that the three pathogens associated with controversy commonly display these symptoms. The Manatsathit et al group advise ruling out STEC by careful stool examination but this takes some time and contravenes the recommendation of early treatment. Nathan et al suggest weighing up potential benefit by treating patients who are not thought to have STEC or resistant Campylobacter without suggesting how this is achieved.

An outbreak is classified as acute diarrhoea in two or more persons from the same exposure, assumed to be caused by the same pathogen. If any of the following pathogens (Salmonella, Shigella, Campylobacter, Cholera or STEC) is yielded from an affected patient then any further patients from the outbreak should be managed for the originally isolated pathogen regardless of severity of symptoms including the empirical antibiotic therapy.

Prevention

Preventative strategies to stop and limit outbreaks are crucial on military operations. The improvement in ablution facilities, the obsessive use of hand washing with soap and water before meals, the use of disposable eating utensils and plates, and strict hygiene rules within health care facilities have all had a major impact on the incidence of this condition.

We use a policy that specifies that discharge from hospital 24 hours after production of a normal stool, or 48 hours with no bowel motion is used within our operational theatres in the hope of limiting outbreaks. In the instance of an outbreak all personnel involved are isolated within one of our facilities. In an operational theatre working with the environmental health officer and infection control nurse allow us to react swiftly to potential outbreaks, and create an environment of discipline to prevent infection.

Treatment Srategy

We present a treatment strategy algorithm based on best available evidence that can be used as a treatment guide for use on operations (Figure 1).

A thorough initial assessment of the patient is the cornerstone in determining the correct therapeutic path. The diarrhoea episode is classified in severity according to the presence or absence of fever, bloody stool or profuse diarrhoea. The presence of any these is an indication for immediate stool culture.

The level of dehydration should be noted, and classified as mild, moderate or severe. Only those classified as severe should automatically receive IV fluids guided by electrolyte monitoring, the remainder should rehydrate with oral fluids unless they cannot be tolerated. In the military environment IV fluids can be used at a lower threshold where personnel are in conditions that are environmentally hostile. Continuing normal diet is recommended where tolerated to assist removal of the organism from the gastrointestinal tract.

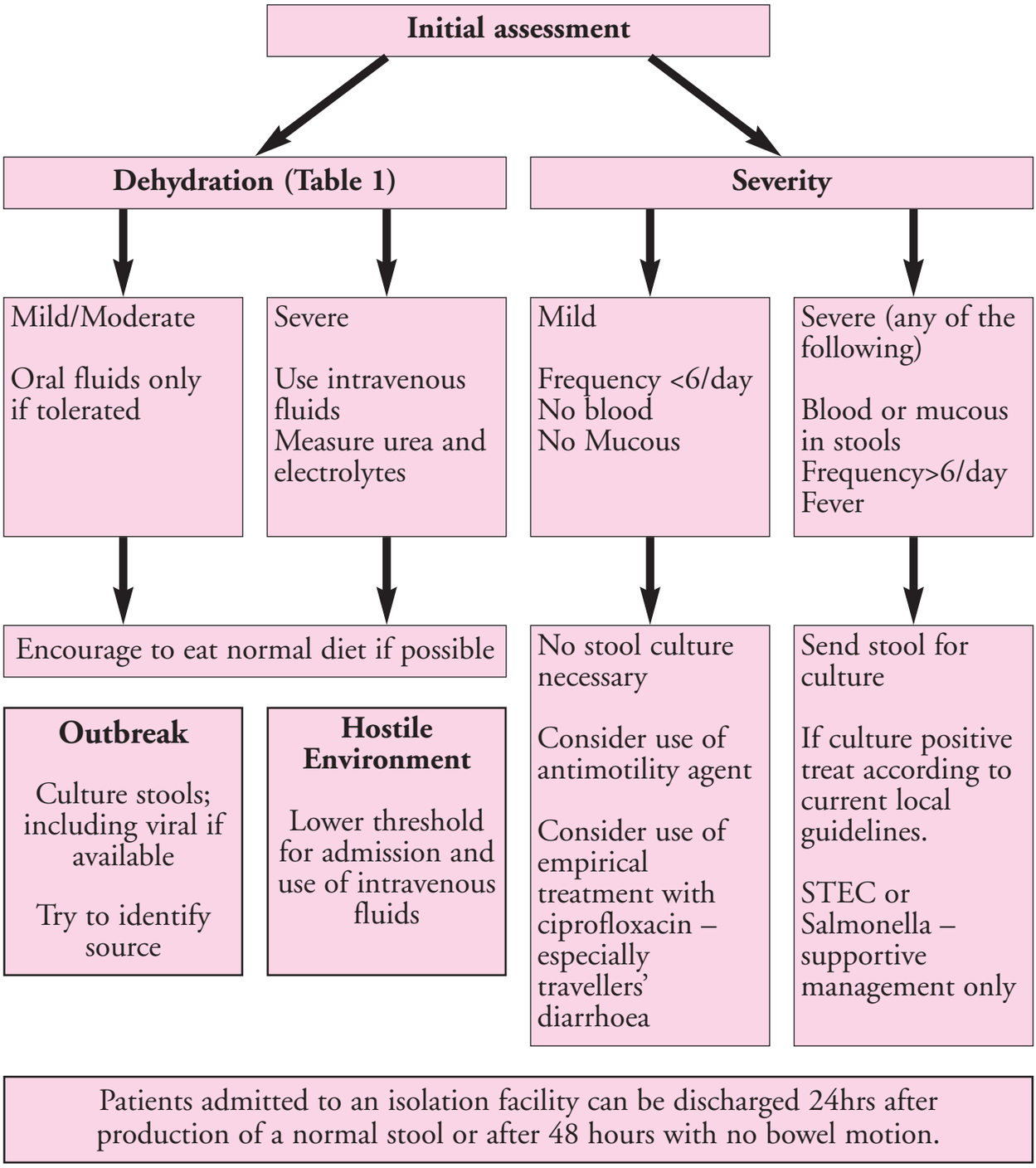

Figure 1. Treatment algorithm for the treatment of acute diarrhoea in healthy adults.

Antibiotic therapy should be considered for isolated pathogens in accordance with regional variance and resistance patterns.

For an outbreak, cultures should be taken including viral if available. Appropriate empirical antibiotic treatment is then given to all affected if a pathogen is isolated. Conservative treatment is the consensus for STEC and Salmonella.

Empirical treatment with ciprofloxacin can be considered for bloody or febrile diarrhoea where Salmonella or STEC is not suspected. For watery travellers' diarrhoea ciprofloxacin should be used for 1 to 5 days, and military personnel newly arrived in theatre (within 2 weeks) with watery diarrhoea should be considered as such. Loperamide is also useful for these patients and for mild cases of watery diarrhoea.

Diarrhoea that lasts more than 7 days should be examined for ova, cysts and parasites and empirical treatment with metronidazole is recommended, especially if previous culture was negative and there is a relevant travel history.

Bibliography

1. Brown, D., Gray, J., Macdonald, P. et al. Outbreak of acute gastroenteritis associated with Norwalk-like viruses among British Military Personnel - Afghanistan. Centres for Disease Control and Prevention. June 2002 p. 477-9.
2. Choi, S.W, Park, C.H., Silva T.M.J, Zaenker, E.I., and Guerrant, R.L. To Culture or Not To Culture: Fecal Lactoferrin Screening for Inflammatory Bacterial Diarrhea. Journal of Clinical Microbiology, 1996. 34(4): p. 928-932.
3. Kosek, M., Bern, C., and Guerrant, R.L. The global burden of diarrhoeal disease, as estimated from studies published. Bull World Health Organ, 2003. 81: p. 197-204.
4. Thielman, N.M., Guerrant, R.L., Acute Infectious Diarrhea. NEJM, 2004. 350(1): p. 38-47.
5. DuPont, H.L., Travelers' Diarrhea: Antimicrobial Therapy and Chemoprevention. Nat Clin Pract Gastroenterol Hepatol., 2005. 2(4): p. 191-198.
6. US centre for disease control and prevention. CDC. 2006.
7. Guerrant, R.L., Van Gilder, T., Steiner, T., Practice Guidelines for the Management of Infectious Diarrhea. CID, 2001(32): p. 331-351.
8. K W Heaton, S.J.L., Bristol Stool Chart, University of Bristol.
9. Dundas, S., Todd, W.T.A, Acute diarrhoea and fever. J R Coll Physicians Edinb 2006; 36:236–240, 2006. 36: p. 236-240.
10. Manatsathit, S., DuPont, H.L., Farthing, M. Guideline for the management of acute diarrhea in adults. Journal of Gastroenterology and Hepatology, 2002(17): p. S54-S71.
11. Health Protection Agency Scotland, Gastrointestinal infections: Laboratory Reports Scotland 1983-2004. 2004.
12. Wingate, D., Phillips, S.F., Lewis, S.J. et al Guidelines for adults on self-medication for the treatment of acute diarrhoea. Aliment Pharmacol Ther, 2001. 15: p. 773-782.