

A Proactive Management Approach to Traveller's Diarrhoea in Vulnerable Travellers

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Individual attributes such as ageing and immune suppression can affect the world traveller. They increase vulnerability of older and immunocompromised people to infection, traveller's diarrhoea. (TD) chronic diarrhoea and irritable bowel syndrome. These high health risk groups could benefit from proactive, pre-travel health management and prophylaxis to reduce exposure to pathogenic invasion of the gut. Bacterial food biosensors, vaccination and pretravel food supplements such as prebiotics may help to reduce travel induced gut infection.

A Frequent Travel-related Illness

TD results from invasive organisms associated with water supply, inadequate sanitation, and poor hygiene. The problem predominates in international tourism, in frequency and personal impact.¹ and has deleterious effects on aged, immunosuppressed people and if there is marked fluid loss with disturbed electrolyte imbalance. Pre-existing impaired renal function in many older travellers makes it difficult to maintain water and electrolyte balance and may increase cardiac arrhythmias, myocardial and cerebral infarction. Vomiting and diarrhoea with fluid and electrolyte imbalance can have an adverse impact on chronic disorders eg. diabetes mellitus and absorption of routine medications may be disturbed in ill and old.³ Elderly travellers are more likely to acquire gastrointestinal infection than younger people, due to lower immunity and decreased protective gastric secretions, with reduced ability to combat infection. If elderly or immuno-compromised travellers become ill from diarrhoea while overseas, delay in access, or inadequate supportive medical services, may bring serious complications. Immediacy of toilet demands from TD concerns elderly sufferers with physical disabilities where toilet access and adequacy are problematic.

TD - a potentially preventable illness

INCREASED VULNERABILITY TO INFECTION

can be due to: Adverse Aging Effects

Loss of function

Ageing organs lose function, with decrease in capacity leading to system malfunction and failure. There is reserve ability to maintain normality, but travel can bring additional physiological demands and infection. Ageing effects on kidney and stomach make older world travellers more vulnerable to travel-related intestinal disease than younger people.² They also often suffer from pre-existing disease and may be less able to compensate for the challenges of hostile environment and infection.

Ageing kidneys bring decline in glomerular filtration rate, decreased urinary concentration, decrease in diluting ability, diminished urinary acidification, impaired potassium clearance, proneness to drug toxicity, and impairment of fluid and electrolyte balance, especially when dehydrated. Ageing increases risk of urinary disorders including acute and chronic renal failure. By age 75, 10% of elders will have sufficient loss of kidney function to be categorised in stage 3A chronic kidney disease.^{4,5}

Immunity

Immunity declines with ageing, with enhanced vulnerability to infectious agents. Causes of immunosenescence include progressive atrophy of thymus gland-affects ability to generate a cell-mediated immune response. The gland - where T lymphocyte ("T cell") immune cells mature, is about 15% of size at adolescence by middle age. T cell number does not decrease with aging, but T cell function does, causing weakening of the immune system controlled by these T cells. Elderly people produce fewer helper T cells. The ones they do have are often less effective than in young.

These changes bring slow, steady decrease in immunity. With body exposure to bacteria or micro-organisms, fewer protective antibodies are formed, or they form slower. Diminution of cell-mediated immune response, leads to progressive reduction in antigen-driven lymphocyte proliferation, a common deficit in elderly individuals. Cellular immunity also declines. The immune system becomes less able to detect foreign particles and infection risk is greater.⁶

Existing disease

Increased vulnerability to infection may result from underlying medical conditions in aged people. Different immune responses may bring different out-comes, eg. susceptibility of aged population to negative effect of cytokines excreted during the disease process may be higher. Illness, surgery and trauma can further weaken the ageing immune system, increasing susceptibility to subsequent infections. Diabetes, can lead to decreased immunity. Elderly people with disorders producing low O₂ levels e.g., COPD, have reduced tolerance to infection.³ Long term medication adds to health risk with potential effect on preventive chemotherapeutic management.³

Gastric secretions

Advanced age is associated with significant alterations in gastric mucosal defence mechanisms and diminished responsiveness to injury and infection. Changes in gastric mucosal defence may impair gastric mucosal prostaglandin synthesis and other protective mechanisms against noxious and infective substances. Gastric secretion from secretors does not decline but, amount decreases due to atrophy of gastric lining.^{7,8,9,10}

Immuno-deficiency effects

in immunodeficiency, immune system ability to fight infection is compromised. The immuno-compromised person is particularly vulnerable to opportunistic infections. immunodeficiencies, can result from immunosuppressive agents, eg. malnutrition, aging and medications (e.g. chemotherapy, disease-modifying anti-rheumatic drugs, immunosuppressive drugs, glucocorticoids. immunodeficiency is a hallmark of acquired immunodeficiency syndrome (AIDS). The virus (HIV) directly infects T helper cells, and impairs other immune system responses indirectly. Many immunodeficiency syndromes present clinical characteristics of autoimmunity. Decreased ability of the immune system to clear infections in these patients may be responsible for causing autoimmunity through perpetual immune system activation. eg. common variable immunodeficiency (CVID) where multiple autoimmune diseases are seen, like inflammatory bowel disease, autoimmune thrombocytopenia and autoimmune thyroid disease.^{11,12,13}

Causes of immunosuppression include:

- immunosuppressant medications a side effect of chemotherapy medications used to treat cancer¹¹
- Corticosteroid medications like prednisone
- inherited diseases
- Acquired diseases like HiV/AiDS
- Asplenia, increasing age, diabetes, and malnutrition¹³

Immunosuppressed people are already at risk in Britain from contaminated food served in restaurants and if personal hygiene is not rigorous. Higher exposure to infected food and drink occurs in visits to developing countries with less personal control over exposure and hand washing facilities may be limited.

Traveller's Diarrhoea

TD - at least three unformed stools, plus sign /symptoms (abdominal cramps, pain) of enteric infection,¹⁴ -ranges in frequency (10-60%) with highest rates in Latin America, Africa and India. Lowest rates (<4%) occur in North America, Western Europe, Japan, Australia and New Zealand travel. Risk is associated with destination, stay duration, travel mode, ingestion of contaminated food or water. 30-50% of travellers will be affected during a one/two-week stay in high-risk areas.¹⁴ with estimates of 50,000 travellers a day affected.¹⁵ Many older travellers return home infected and seek treatment from GPs.¹⁶ Mortality is uncommon but, 1% of people require hospital admission.^{17,2} in perspective, acute non-travel-related diarrhoea (NTRD) of infective origin affects 20% of England's population annually, 1 in 6 seek GP treatment. About 6% of adults report an acute attack in a preceding two week period, at home.¹⁷

Professional management of acute episodic diarrhoea varies and doctors often delay therapeutic intervention, or limit prescription of appropriate medication.¹⁸ Affected people who consult a doctor are likely to be older, in poor health and taking regular medication.

Causes

20-40% cases are due to undetected bacterial enteropathogens with up to 80% caused by E. coli. Vomiting predominates in 10%, often norovirus infection, or ingestion of preformed toxin of Staphylococcus aureus, from contaminated food.¹⁹ Vomiting plus diarrhoea leads to dehydration, electrolyte imbalance and renal failure in old and immunocompromised people.²⁰

Proactive intervention

Advice

Preventive measures emphasise avoidance of potentially contaminated food / drink and hand-washing before eating and drinking and after toilet visits. "Boil it, cook it or avoid it" is a useful adage if people would follow the practice. Adherence to instructions and compliance by travellers is universally poor. Only 4 in 5 people wash hands after toileting and only 5% wash sufficiently to destroy bacteria, with men poorer than women in hand hygiene.²¹

Health professionals have ambivalent attitudes to TD prevention and reluctance to prescribe anti-diarrhoeal medication. Many believe that "anti-diarrhoeals keep toxins or pathogens inside the intestine where they do more damage to the gut, and prolong illness by delaying excretion of pathogens," a premise unsupported by research based evidence. Few recommend preventive pretravel anti-diarrhoeal medication. A third of GPs would take no action for 24 hours, with 12% delaying for 48 hours in TD.²² a response disadvantageous to vulnerable groups.

Patients have a more robust response than professionals when afflicted. Two thirds of actively treat their diarrhoea, with half self-medicating.²²

Vaccination

Vaccination is of limited value providing short-term protection only (approximately 3 months) against ETEC diarrhoea, but BS-WC vaccine may be considered for those with chronic illnesses e.g., chronic renal failure, congestive heart failure, insulin-dependent diabetes mellitus, inflammatory bowel disease. Efficacy against ETEC diarrhoea is 52% and overall protection against travellers' diarrhea 23%.

Antibiotics

Pretravel antibiotics bring concerns about resistance and side effect, particularly in the old, but may be considered for vulnerable older and immunocompromised people travelling to remote high risk areas. Cost benefit analysis of treatment with doxycycline or ciprofloxacin showed them however to be more cost effective than prophylactic use of these drugs.

Prebiotics

Pretravel prebiotic ingestion is relatively free of adverse reaction.²⁴⁻²⁸ Second generation prebiotic food supplements taken prior to and during travel, may help prevent or diminish TD. Prebiotics are selectively fermented ingredients allowing specific changes, in composition and/or activity, in gastrointestinal micro-flora conferring benefits upon host well-being and health. Current prebiotics are non-digestible, short chain, carbohydrates, which alter composition and/or metabolism of gut micro-flora in a beneficial way. Mainly oligosaccharides (OS) and non-starch polysaccharides, they provide nourishment and promote growth and/or activity of probiotic bacteria in the large intestine and affect intestinal bacteria by increasing number of beneficial anaerobic bacteria e.g. bifidobacteria and decreasing population of potentially pathogenic microorganisms e.g. clostridia.^{24,29} They arrive relatively unchanged in the gut.²⁴ Prebiotics stimulate preferential growth of a limited number of health-promoting commensal flora already residing in the colon.³⁰

Second generation prebiotics may have a:

- Direct positive effect on Bifidobacteria and microflora balance to reduce pathogenic colonisation by presence of beneficial microflora
- Direct antimicrobial effect -adhering to receptors on intestinal binding sites and by mimicking these receptors, block adhesion of pathogens to intestinal epithelial cells
- Synergistic positive effect on immune function, indirectly due to positive change in microflora and reduction of pathogenic bacteria present, directly by interacting with immune cells and affecting various intercellular pathways.²⁸

Fructan type OS and galactooligosaccharides (GOS) predominantly increase the number and/or activity of bifidobacteria and lactic acid bacteria.²⁸ and potentially could reduce the risk of gastroenteritis and infections. Evidence of value in travellers' diarrhoea is limited.^{31,5} New technological advances are improving functional properties of prebiotics. Second generation GOS work, by highly selective proliferation of beneficial bacteria, blocking invasion of pathogens and as immunity modulators. They target specific bacterial species and offer added functionality (i.e. immune function and anti- and pathogenic activity).

As galactosidase originates from bifidobacteria, B-GOS has a better bifidogenic effect than other GOS.²¹ it has a significantly better effect in reducing incidence duration and severity of diarrhoea compared to placebo.³⁶ ingestion showed significantly increased bifidobacteria levels and direct positive effect on immune system with a positive effect in an elderly cohort.²⁷ it also strongly inhibited attachment and colonisation of gastrointestinal pathogens ETEC and Salmonella typhimurium.

B-GOS inhibit adhesion of gastro-intestinal pathogenic bacteria in small intestine, change pH in large intestine with positive change in microflora, have indirect positive effect on immune system through significant increase in beneficial bacteria. They have a positive direct effect on the innate immune system from increased natural killer (NK) cell - cytotoxic lymphocytes that constitute a major component of the innate immune system-and phagocytic activity and the adaptive immune system from increase in anti-inflammatory cytokines and decrease in pro-inflammatory ones.^{37,38} Potentially they could be a useful pretravel dietary adjuvant for the older world traveller, those with lowered immunity, those vulnerable to gastro-intestinal infection.^{39,40,41} ingestion does not increase health risk.⁴² Meta-analysis of trials using probiotics for gastroenteritis report flatulence and abdominal bloating adverse effects and are safe other than with the severely immuno-compromised.^{43,44-47}

Food protection

Conventional pathogen detection methods rely on microbiological and biochemical analysis, which are accurate but time consuming, and not amenable to on-site diagnosis. Enhanced detection technologies with high levels of reliability, sensitivity, and selectivity and a real-time biosensing system to detect pathogenic bacteria are needed. Biosentinels, used to detect, signal, and capture pathogenic bacteria, are based on magnetically soft magneto-elastic resonators coated with a selective and specific biorecognition layer. These are actuated, monitored, controlled wirelessly by external magnetic fields. They mimic the function of naturally occurring biological defensive systems, such as white blood cells, seeking out and capturing pathogenic bacteria.

After binding with target pathogen, the mass of the biosentinel increases causing the resonant frequency to decrease, providing instantaneous detection of the pathogen. Hand-held scanners that detect whether a meal contains traces of bacteria are in development. They can be passed over food before it is served to determine if its surface is contaminated with bacteria or viruses. False positive and false negative signals delay universal application. If effective their use on food presentations would greatly reduce diarrhoea from infected food and water.⁴⁸

Conclusion

Improved sanitation, personal hygiene and bacterial identification will ultimately decrease food and water contamination and infective risk to travellers. Vaccines promise effective prevention.⁴⁸⁻⁵¹ Avoidance of infected foods /water and good personal hygiene remain crucial in prevention. Antibiotics have a place.⁵² Second generation prebiotics have potential to protect vulnerable older travellers, those with lowered immunity and travellers to high risk areas. Further research is required to confirm their value. Health professionals should consider proactive, pretravel management in the elderly and immunosuppressed to reduce infection and morbidity.

Management Plan

- identify elderly and immunocompromised travellers and those at higher health risk
- Assess TD risk
- Advise traveller of diarrhoea risk
- Advise on importance of food and water risk and appropriate prophylaxis
- Emphasise need for pre eating and post toileting, adequate hand- washing
- Augment information with a hand-out leaflet.
- Suggest appropriate vaccination, pretravel prebiotics and first-aid anti-diarrhoeal medication

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