Gastrointestinal Drugs in Aircrew

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INTRODUCTION

Gastrointestinal diseases (GID) are common disorders in the general population. More than 50% of patients presenting with GID complaints are in the decades of life typical of military personnel, and GID represent some of the commonest reasons for medication waivers in military aircrew. The clinical course of most gastrointestinal disorders tends to be chronic, with unpredictable remissions and relapses, and a propensity for complications which may be acutely disabling or may chronically worsen the individual's general health. The development of GID by aviation personnel often leads to variable degrees of limitation in their flying duties, largely depending on the natural history of the disorder. The most common GID of aeromedical interest are: gastroesophageal reflux; peptic ulcer, both gastric and duodenal; chronic inflammatory disease of the bowel, predominantly regional enteritis and ulcerative colitis; and irritable bowel. Pharmacologic agents to treat GID include many of the most commonly used drugs in medicine, including antacids, histamine H2-receptor blocking agents, anticholinergics, proton pump inhibitors, antimotility agents, and antibacterials.[1]

Gastroesophageal Reflux (GER)

Heartburn is probably the commonest GER symptom. When heartburn and acid regurgitation become regular and persistent, appropriate medical therapy is necessary. Mild to moderate GER responds well to lifestyle advice and acid suppression.[2] To neutralize acidity, non-absorbable antacids such as magnesium and aluminum hydroxides are preferred, being associated with few side effects; diarrhea, the commonest, usually does not occur at a total daily dose <90ml. To reduce acid secretion, an H2 antagonist such as ranitidine 300 mg/day, or a proton pump suppressant[3] such as omeprazole 20-40 mg/day, may be used. Cholinergic agents such as domperidone,[4] cisapride, or metoclopramide may also be used to increase sphincter pressure.[5] Cessation of acute therapy after 4-8 weeks is associated with relapse in 70-80% of patients; thus, maintenance therapy such as ranitidine 150 mg/day is commonly employed for at least one month longer.

Aeromedical Concerns

GER normally responds well to medical therapy in 4-8 weeks. After the acute phase, subjects with mild to moderate disease may be fit to fly with appropriate limitations. For severe GER, flying, especially high performance aviation, may be a provocative factor and is contraindicated. Maintenance therapy with ranitidine or omeprazole is compatible with a return to unrestricted flying duties. Therapy with a prokinetic agent such as cisapride or metoclopramide is not, because of serious sedative and extrapyramidal side-effects.[6,7]

Peptic Ulcer (PU)

PU occurs most commonly in the proximal duodenum and along the lesser curvature of the stomach. Duodenal ulcer is commonest in young males. Both duodenal and gastric ulcers have a remitting/relapsing natural history and can be associated with serious complications, such as hemorrhage and perforation. Although the secretion of acid or pepsin into the stomach is the proximate cause of peptic disease, the great majority of cases are associated with *Helicobacter pylori* (Hp) gastritis. Hp is present in 90% of duodenal and 60-70% of gastric ulcers. Recent data show that in patients followed for three years after ulcer healing, eradication of Hp with antibiotics may prevent ulcer relapse in 80-87% of individuals. The goals of medical therapy are suppression of acid secretion and Hp eradication. H2 receptor antagonists and proton pump suppressors are used.[8] Cimetidine, 800 mg/d, ranitidine, 300 mg/d, famotidine, 40 mg/d, or nizatidine, 300 mg/d, lowers gastric acidity and promotes healing of duodenal and gastric ulcer in

4 to 8 weeks. Omeprazole, 20-40 mg/d, lansoprazole, 15-30 mg/d, or pantoprazole, 40 mg/d, can completely inhibit acid secretion and has a long duration of action; healing typically occurs in 100% of cases within 2 to 4 weeks. Additional agents include sucralfate,[9] which forms a protective coating in the base of ulcer, and bismuth-containing preparations, which have an action similar to that of sucralfate. Eradication of Hp can be achieved using antibacterial therapy, but antibiotic regimens are complex; the best regimen is a matter of debate which is beyond the scope of this monograph, particularly since the aviator would likely remain grounded during treatment.

Aeromedical Concerns

Aircrews suffering from PU require at least two months grounding for uncomplicated cases. At the end of this period, during which patients are unfit for flying duties, endoscopic evaluation must confirm the complete healing and eradication of Hp.[10] When both goals are successful, subjects have a very small risk of relapse and may return to unrestricted flying duties. All H2 antagonists have side effects of potential concern, such as drowsiness, tiredness, dizziness (cimetidine), vertigo, headache, diarrhea (ranitidine), fatigue (famotidine), asthenia, and sleepiness (nizatidine).[11,12] Several studies with evaluation of visual and motor performances, alertness and behavior, did not show any interference by cimetidine or ranitidine, suggesting that the use of H2 antagonists in aircrews should be limited to those two drugs.[13,14] Side-effects of proton pump suppressors,[15] such as visual disturbances (omeprazole) and, rarely, necrotic arthritis (lansoprazole), are of concern for flying personnel, and less information is available about these drugs. In cases complicated by hemorrhage or perforation, flying must be forbidden for one year, and endoscopic evaluation will be necessary at the end of that period. If Hp infection was documented and the organism is shown to be eradicated, the risk of future complications should be low.

Inflammatory Bowel Disease

Regional enteritis (Crohn's disease) and ulcerative colitis are characterized by chronic inflammation which may occur in any part of the gastrointestinal tract and have a natural history of remissions/ relapses. Both conditions may significantly compromise aviation personnel employability and always require full specialist evaluation.

Regional Enteritis (RE)

RE commonly affects the distal ileum and colon, but the entire small bowel may be involved. Most cases begin before age 40 and occur about equally in both sexes. RE is characterized by lifelong exacerbations, with a recurrence rate of almost 100% within 15 years.[16] Chronic diarrhea, associated with abdominal pain and fever, is the usual presenting symptom. Complications, both local and extraintestinal, are common, and include fistulas, abscesses, malabsorption, anemia and arthritis. No specific therapy exists. Antidiarrheal agents, such as loperamide (2-4 mg/day), may be used to relieve cramps and diarrhea. Aminosalicylate preparations are useful in suppressing mild or moderate disease, maintaining remissions, and preventing relapses; both sulfasalazine and mesalazine (known as mesalamine in the USA) should be administered with a low initial dosage (500 mg or 400 mg, respectively), then gradually increased up to 4-8 g or 2.4-4 g daily in divided doses, respectively.[17,18] In acute stages of disease, systemic corticosteroid therapy is usually added, such as oral prednisone, 40-60 mg/day, with gradual dosage reduction depending on response. Surgical intervention is mandated when recurrent intestinal obstruction or serious complications, such as fistulas or abscesses, are present.

Aeromedical Concern

A diagnosis of RE usually leads to a period of temporary grounding for a minimum of several months. In those cases in which remission is maintained for a prolonged time, a return to limited flying duties can be considered. Those subjects suffering from small intestine enteritis are usually assigned to restricted duties, and are generally unfit for solo-pilot. Others with uncomplicated RE limited to the colon and with remission for at least one year may return to less restricted flying categories. During maintenance therapy, aircrews may often need to be grounded because of side-effects of medical therapy, which are frequently dose-related. In up to 30% of subjects sulfasalazine may cause significant side effects such as vomiting, nausea, anorexia, headache, cutaneous rash, hemolytic anemia, blood dyscrasia, and, rarely, hepatitis. Mesalazine as a rule is usually better tolerated.

Ulcerative Colitis (UC)

UC is a chronic ulcerative disease involving the entire colon, and is characterized by frequent attacks of bloody diarrhea and repeated exacerbations and remissions. UC is more common in males and in the young, peaking between 15 to 30 years of age. Diarrhea attacks may present with varying intensity and duration. Hemorrhage and fistulas are common local complications; peripheral arthritis, uveitis and episcleritis are also common and emphasize the systemic nature of this disease. Colonoscopy and biopsy are useful to assess the extent of disease and distinguish ulcerative from regional (Crohn's) colitis. The therapeutic approach is similar to that used with RE.[19] Antidiarrheal agents, such as anticholinergics, loperamide, or codeine, may lead to symptomatic improvement, but should be used with extreme caution. Mild to moderate disease may respond to mesalazine or sulfasalazine. Severe disease requires systemic corticosteroid therapy with oral prednisone. Nearly a third of patients with extensive disease eventually require surgical extirpation of the colon.

Aeromedical Concern

A diagnosis of UC is cause for temporary grounding for a period of 6 months. Those patients in whom disease is restricted to the rectum or distal sigmoid, and show clinical remission without any evidence of complications or drug side-effects, may be returned to limited flying duties, usually restricted to flying in multi-crew aircraft. Serious and extensive disease, because of a significant incidence of complications and relapses, should be considered incompatible with flying.

Irritable Bowel Syndrome (IBS)

IBS is a very common clinical syndrome, representing about 50% of all gastrointestinal complaints. Motility disorders are associated with a variety of symptomatic presentations, most commonly abdominal pain, diarrhea, or constipation. By definition, no anatomic cause can be found, and the condition commonly represents a reaction to stress, emotional factors, diet, or occasionally drugs in susceptible individuals. In many cases, reassurance is all that is required. Regular physical activity is indicated to relieve stress, and a diet high in insoluble fiber may improve bowel function. Pharmacotherapy is usually indicated only in severe cases. In patients with diarrhea, loperamide (2-4 mg) may be given before meals. To relieve spastic symptoms, anticholinergic agents and a mild sedative may be temporarily used.

Aeromedical Concerns

The severity of symptoms can vary widely. IBS is usually compatible with flying, but severe and persistent symptoms, especially those requiring drug therapy, may require grounding.

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