CHAPTER 103

Gastrointestinal Problems in Acute Kidney Injury

Susie Q. Lew and Todd S. Ing

OBJECTIVES

This chapter will:

1. Present an overview of the epidemiology, pathogenesis, and clinical features of common gastrointestinal problems associated with acute renal failure.
2. Describe the management of common gastrointestinal problems associated with acute renal failure.

The second half of the 20th century saw remarkable changes in the clinical presentation of patients suffering from acute renal failure (ARF). These changes relate to the emergence of new nephrotoxic agents, the change in pattern of ARF-inducing diseases, and improvement of medical care through use of more effective drugs and the earlier application of efficient renal replacement therapies. Because patients with untreated terminal ARF are encountered rarely, some of the advanced gastrointestinal (GI) complications of uremia,

such as stomatitis and colitis, for example, are seen less frequently than in years past. Nevertheless, certain other GI complications, such as bleeding, still warrant close attention. Furthermore, uremia-induced GI symptoms such as anorexia, dysgeusia, nausea, and vomiting continue to plague patients and often herald the need for prompt renal replacement therapy.

PATHOGENESIS OF UREMIC LESIONS IN THE GASTROINTESTINAL TRACT

The entire GI tract may be involved in advanced uremia, with the stomach and the small and large intestines affected most commonly. Jaffe and Laing[1] found the earliest pathologic changes in the GI tract of uremic patients to be in the form of capillary hyperemia, dilatation of submucosal veins, edema, hemorrhage, and subsequent bacterial invasion of the devitalized areas, accompanied by fibrinous exudates and necrosis.

Urea retention can impair gastric defense against autolysis. Edward and Skoryna demonstrated that an increase in gastric juice urea level may lead to dissolution of gastric mucus.[2] In addition, by investigating ionic fluxes across the stomach of experimental animals, Davenport[3] found that intraluminal urea in high concentrations could raise gastric permeability. A consequence of this gastric hyperpermeability is an augmented back-diffusion of hydrogen ions from the gastric lumen to the mucosa. Fisher et al.[4] observed that gastrin could cause pyloric incompetence by antagonizing the effects of cholecystokinin and secretin on the pyloric sphincter. Gastrin is catabolized by the normal kidneys. With ARF, gastrin catabolism is impaired and plasma gastrin level commonly rises.

Wesdorp et al. observed a nearly sixfold increase in the mean plasma gastrin level in patients with ARF as compared with control subjects, with levels in approximately 20% of the patients reaching levels in the Zollinger-Ellison range.[5] Although an elevated plasma gastrin level may foster GI bleeding and gastritis, intragastric pH is not lower in patients with renal failure. Indeed, a low basal acid output with a high basal intragastric pH, but with a significant peak acid output, has been found in patients with ARF.[5] Moreover, pentagastrin-stimulated gastric acid secretion is normal in patients with ARF.[5] The high basal intragastric pH may reflect the neutralizing effect of a high gastric ammonia concentration. Lieber and Lefevre detected higher gastric ammonia values and lower acid levels in uremic patients as compared with normal control subjects.[6] Gastric ammonia levels are higher as a result of the splitting of the available higher-than-normal amounts of urea by urease-rich bacteria in the stomach. Impairment of cell renewal and cell division in ARF may reduce the competence of the mucosal barrier, contributing to the initiation and persistence of a uremic lesion by impairing epithelial wound healing.[7]

GASTROINTESTINAL PROBLEMS COMMONLY ASSOCIATED WITH ACUTE RENAL FAILURE

Dysgeusia, Anorexia, Dyspepsia, Hiccups, Nausea, and Vomiting

In uremic patients, dysgeusia commonly manifests as a metallic or a foul taste in the mouth. In addition, anorexia, dyspepsia, hiccups, nausea, and vomiting are frequent components of the uremic syndrome. Persistent vomiting may bring about dehydration (with associated dryness of the tongue and of the mouth), electrolyte disturbances, and wasting.[8] With regard to therapy for nausea and vomiting, apart from dialysis, symptomatic improvement can be obtained with phenothiazines or metoclopramide, given either parenterally or rectally.

In hemodialysis patients, maintaining a blood urea level above 50 mmol/L (300 mg/dL) for periods of 7 to 90 days through the use of a urea-enriched dialysis solution can bring about vomiting.[9] A rapid reduction of a very high blood urea level can lead to a constellation of manifestations known as the *dialysis disequilibrium syndrome* (DDS). Salient features of the syndrome include nausea and vomiting. DDS is believed to be the consequence of cerebral edema engendered by either the entry of water into brain cells during dialysis, secondary to the rapid decline in extracellular fluid osmolality, or by the induction of a dialysis-induced acidosis of the cerebrospinal fluid and of the brain.[10]

Stomatitis, Uremic Fetor, and Inflammation of Salivary Glands

In advanced uremia, uremic stomatitis, characterized by a red, thickened buccal mucosa with a superimposed gray, thick, and gluey exudate, can occur.[11] Ulcerations also are a prominent feature in some patients. Stomatitis and glossitis, often accompanied by a dry burning mouth, commonly are associated with poor dental hygiene. Patients with advanced uremia may exhibit the fetor of uremia (uremic odor) in addition to uremic stomatitis. The fetor of uremia is an ammoniacal odor, reminiscent of that of stale urine.[8] The suggestion has been made that large amounts of ammonia are formed as a result of the action of bacterial urease on urea, present in high levels in the saliva of uremic patients. The ammonia so produced is suspected to be the cause of the stomatitis.[8] Inflammation of the salivary glands (e.g., parotitis) also may occur in uremic patients, often in association with stomatitis.[8]

Gastrointestinal Hemorrhage

In the early part of the last century, acute GI hemorrhage was a dreaded complication in patients with ARF. Indeed, before the 1970s, GI bleeding, occurring in as many as a third of these patients, was the second leading cause of death.[12–15] Subsequent reports indicate a fall in the incidence of such bleeding. For example, in a 1978 study involving 276 patients with ARF, GI bleeding was seen in 90 patients (33%). The bleeding was mild and readily controlled in 75 of these patients, however, four patients died from the GI bleeding (1.5%).[16] In addition, in a series of 636 patients with ARF treated between 1980 and 1989, only one of 214 deaths was attributed to GI bleeding.[17] The dearth of GI hemorrhage as a cause of death in ARF in more recent years may be related to prophylactic therapy with effective acid-lowering regimens,[18] as well as to the better control of uremic bleeding by prompt and effective renal replacement therapies.[17,19,20]

Although many earlier-published reports apparently supported the notion that a fall in the incidence of GI bleeding among patients with ARF had occurred in the recent past,[17,19,20] a 1997 investigation nevertheless described an 8% to 13% incidence of GI bleeding among patients with ARF.[21] Furthermore, a 2001 study also reported a 13%

incidence of acute GI bleeding as a complication of ARF. In this prospective study, involving 514 patients with ARF, GI bleeding occurred despite prophylaxis with ranitidine therapy. In most cases, the bleeding was the result of upper GI disease. In 48 endoscopic procedures performed, gastric erosions or ulcers were found in 42% of the patients, duodenal ulcers in 12%, esophageal varices in 11%, and gastric neoplasia in 6%. The severity of the underlying illness, the intensity of the uremia, a low blood platelet count, and the presence of hepatic disease were found to be significant risk factors.[22] According to the study investigators, acute GI bleeding in patients with ARF is a risk indicator of increased health resource utilization and death.[22] The aforementioned gastric erosions and ulcers, along with duodenal ulcers, are likely to be the manifestations of stress-related mucosal disease (SRMD), a continuum of conditions spanning stress-related injury (superficial mucosal damage) to stress ulcers (focal deep mucosal damage).[18] Whether an element of concomitant uremic gastritis also was present, leading to bleeding from the gastric erosions, however, has not been ruled out.

Stress ulcer and gastritis are common among patients with ARF.[23] Myriad studies have suggested that patients suffering from ARF do not belong to a homogeneous group,[24] and bleeding-prone GI (including hepatic stress-related mucosal disease) diseases that occur in patients who do not have ARF also can afflict patients with ARF.[22] The difference in disease mix and a host of other variables such as age, gender, ethnicity, nutrition status, ARF cause (nephrotoxic, hypoperfusion-related, or a combination of both),[24] severity of bleeding, disease acuity, severity of uremia, comorbidity (such as sepsis, disseminated intravascular coagulation, hepatic failure, diabetes, hypertension, or cardiac disease), and treatment regimens, are likely to be the reasons why the incidence of GI bleeding varies widely among studies involving patients with ARF. Finally, bleeding originating from the lower intestinal tract is not an infrequent terminal event in uremic patients.[8] Under such circumstances, it is likely that uremic enterocolitis is the main cause of the bleeding episode.

Presumed to be a result of a variety of factors, including those of gastric acid, mucosal ischemia, and bile reflux, SRMD most often is seen in critically ill patients in the intensive care unit (ICU) setting.[18,25] Although the cost-effectiveness[26] or even the necessity[27] of SRMD prophylaxis in all critically ill patients in general is uncertain, such an approach using antacids (see later), sucralfate (see later), histamine H_2 blockers, or proton pump inhibitors often has been practiced.[18,25–29] In this regard, most authorities are of the opinion that prophylaxis against SRMD may reduce major bleeding but has not yet been shown to improve survival.[18] Patients at very high risk for the development of SRMD are those with prolonged mechanical ventilation and coagulopathy. Additional risk factors include sepsis, renal failure, hepatic failure, hypotension, trauma, burns, and myocardial infarction. Therefore it has been suggested that ARF patients, especially those who also suffer from coagulopathy or are mechanically ventilated, certainly should receive SRMD prophylaxis to prevent GI bleeding.[18,26]

H_2 receptor antagonists can be used for prophylaxis of SRMD but are not all equally potent. Some of these agents (e.g., cimetidine) have a long list of drug interactions and can cause neurologic and hematologic side effects.[30] A potent H_2 receptor antagonist with minimal drug interactions such as famotidine may be used, but the development of tolerance to H_2 receptor antagonists remains a concern.[30] Garnering increasing popularity, proton pump inhibitors are the most potent antisecretory agents, inhibiting the gastric H^+,K^+-ATPase in the parietal cells and capable of raising gastric pH to above 6.[29,30] Pantoprazole, lansoprazole, and esomeprazole are available in many countries in intravenous formulations. Such intravenous formulations with long-lasting antisecretory effect and little risk of drug interactions are ideally suited for use in the ICU. Finally, when H_2 receptor antagonists and proton pump inhibitors are discontinued, the dosage should be tapered gradually, or the drugs should be substituted with alternatives (e.g., antacids) to prevent acid rebound.[30]

Chromium labeling studies have indicated that even in the absence of overt bleeding, uremic patients have increased GI blood loss when compared with control subjects.[31] Such minor blood loss in the absence of any demonstrable histopathologic lesions may be the consequence of a generalized bleeding tendency secondary to a uremia-induced defect in platelet aggregability and in platelet–vessel wall interaction.[32] This bleeding tendency is reflected in the presence of a prolonged bleeding time.[32]

GI bleeding appears to increase during the hemodialysis procedure and may be compounded by several factors in addition to the use of anticoagulants. During hemodialysis, gastric acid secretion rises whenever blood pressure falls, and this gastric acid hypersecretion may contribute to the higher incidence of GI bleeding.[33] Moreover, intradialytic hypotension resulting from excessive ultrafiltration or other causes can precipitate bowel infarction with resultant GI bleeding.[34] GI bleeding can worsen preexisting azotemia by engendering a hypovolemia-induced reduction in renal perfusion and therefore in glomerular filtration.[35] Absorption of blood proteins from the GI tract, followed by the catabolism of those absorbed proteins by the liver to form urea, probably also plays a role in aggravating azotemia.[36]

Conventional treatment for patients with ARF-related upper GI bleeding has included nasogastric suction, blood transfusion, and the administration of an antacid, sucralfate (see later), an H_2 receptor antagonist, or a proton pump inhibitor. The use of antacids is labor intensive and not popular because of the large amounts required[18] and because of the generally inadequate results.[30] Also, the administration of aluminum-based sucralfate to patients with renal dysfunction can lead to hyperaluminumemia.[37] Although therapy with aluminum-containing drugs (such as aluminum-based antacids and sucralfate) in these patients at conventionally given doses and for a short duration has not been reported to be overtly detrimental, it would seem prudent to avoid the use of such agents because of the risk of hyperaluminumemia. With regard to other antacids, use of magnesium-based preparations is discouraged because of the possibility of hypermagnesemia. Administration of desmopressin,[38] cryoprecipitate,[39] or conjugated estrogen[40,41] can help to reduce GI blood loss in uremic patients with a prolonged bleeding time. Raising the hematocrit level by blood transfusion can shorten bleeding time,[42] probably by enhancing the ability of platelets to adhere to the vascular endothelium.

Dialytic therapy also can shorten the prolonged bleeding time and curtail the bleeding.[43] Kleinknecht et al. were among the first to suggest that dialysis could curb uremic bleeding.[14] In a controlled prospective study of intensive versus nonintensive dialysis in patients with ARF, although overall morbidity and mortality were not different, intensively dialyzed patients suffered fewer hemorrhagic complications.[44]

Finally, a consultation with a gastroenterology specialist who is conversant with diagnostic and hemostatic endoscopic procedures should be obtained promptly for the uremic patient with active GI bleeding.

Hemodialysis treatment in the presence of GI bleeding should be performed without systemic anticoagulation (e.g., up to 7 L of saline introduced into the arterial blood line over a dialysis session in the case of a heparin-free protocol[45–47] or a regional citrate anticoagulation regimen using either a calcium-free or a calcium-containing dialysis solution).[45,46,48,49] Similar anticoagulation techniques also have been used for continuous renal replacement therapies (CRRTs).[46,49] With respect to anticoagulant-free dialysis, the use of saline flushes, 100 mL every 30 minutes, along with the administration of reduced doses of dalteparin has not been found to be effective.[50] The recently introduced method of using low-dose citric acid (0.8 mM [2.4 mEq/L] of citrate in the final dialysis solution) as an acidifying agent for the "acid concentrate" in a dual-concentrate, bicarbonate-based dialysate delivery system may help to reduce the extracorporeal circuit requirement for anticoagulants.[45,51,52]

Patients receiving total parenteral nutrition (TPN) and those requiring broad-spectrum antibiotic therapy are at risk for the development of vitamin K deficiency, hypoprothrombinemia, and resultant bleeding. Prophylactic vitamin K therapy often is indicated, especially in high-risk patients with ARF receiving TPN or broad-spectrum antibiotic therapy.[53–56] In general, the optimal dose of vitamin K has not been established. For TPN, an intravenous dose of 1 mg/day was found to be effective.[54] For antibiotic therapy, most patients will require a dose of 5 to 10 mg orally or subcutaneously once to three times weekly, although as much as 10 mg/day may be necessary.[55] It is preferable to administer vitamin K subcutaneously or intramuscularly, because intravenous administration has been associated with severe reactions resembling anaphylaxis.[56]

Gastritis, Duodenitis, and Peptic Ulcer Disease

In patients with ARF, apart from the SRMD involving the stomach and the duodenum mentioned previously, a progressively diffuse erosive gastritis with thinning of the mucosa and bleeding also has been described.[8] Gastritis and duodenitis presenting as superficial mucosal lesions also can be associated with the use of ulcerogenic drugs such as salicylates, corticosteroids, nonsteroidal antiinflammatory drugs, and iron.[57] Fatal hemorrhage may result from these lesions. It is unclear whether peptic ulcer disease is more common among patients with ARF.[58] Noteworthy is the fact that the raised blood urea levels in uremic patients have not been found to interfere with the urease-based tests used in the detection of *Helicobacter pylori*.[59]

Treatment of gastritis, duodenitis, and peptic ulcer disease is similar to that described previously for the prophylaxis of SRMD. In patients with ARF who have active gastritis, duodenitis, or peptic ulcer disease, the anticoagulation methods used for renal replacement therapy in the face of GI bleeding, as described, also should be applied.

Pancreatitis

The pancreas, like the kidney, is susceptible to ischemic necrosis.[60] Autopsies of patients dying from oligemic shock showed a 50% incidence of major pancreatic injury in those with concomitant ARF, but only a 9% incidence in those without. Similarly, patients dying after nonoligemic shock had a 35% incidence of major pancreatic injury if acute tubular necrosis also was present but only a 12% incidence of pancreatic ischemic injury in the absence of acute renal lesions.[60]

The serum total amylase concentration (a summation of amylases produced by the pancreas, the salivary glands, and other tissues) rises in renal failure, but the value usually does not exceed three times the upper limit of normal.[61] Serum lipase activity is elevated (as high as twice the upper limit of normal) in approximately 50% of patients undergoing dialysis in the absence of pancreatitis.[61] Serum lipase activity increases after hemodialysis as a result of a heparin-induced release of endothelium-bound lipoprotein lipase. Consequently, only predialysis serum samples should be used for the determination of the enzyme.[61] In patients with pancreatitis, with or without renal failure, the serum levels of total amylase, pancreatic P3 isoamylase (P refers to pancreatic), total lipase, and pancreatic lipase levels frequently are elevated markedly. Because P3 isoamylase and pancreatic lipase are of solely pancreatic origin, the magnitude of their levels serves as a more valuable diagnostic pointer. Nonelevated serum levels of these two enzymes often suggest that the diagnosis of pancreatitis is less likely.[62] In patients with renal failure and acute pancreatitis, the total amylase and the pancreatic P3 isoamylase levels in the serum often are elevated markedly. If, however, a substantial amount of pancreatic tissue has been destroyed from prior disease, serum pancreatic enzymes may not be elevated at all in spite of current acute pancreatitis. The diagnosis of acute pancreatitis in the setting of ARF should be based on a combination of clinical evidence as well as elevated lipase and amylase values. Finally, serum amylase activity may be spuriously low in peritoneal dialysis patients using icodextrin-based dialysis solutions, on account of the interference of icodextrin with amylase measurement.[63]

Cholecystitis

A high incidence of acute acalculous cholecystitis in critically ill patients with ARF has been reported.[64] Some of these patients may suffer from biliary peritonitis, a complication of gallbladder rupture. The diagnosis can be difficult and requires a high index of suspicion in addition to ultrasonography. Biliary drainage often is necessary for treatment.

Enterocolitis and Other Colonic Problems

Uremic enterocolitis has been described in the form of necrotizing ulcers in the lower part of the small bowel and the large bowel, particularly in the lymphoid tissue. Severe diarrhea with purulent or bloody stools may be a feature.[65] Apart from uremia, whether such intestinal pathology is related to a secondary bacterial infection also is unknown.[8] Uremic "colitis," characterized by diarrhea that cannot be attributed to other causes, is one of the terminal complications of uremia (but is a rare event in ARF).[66] Patients with uremic enterocolitis may present with an acute abdomen[67] with pain, rigidity, and tenderness, as well as nausea, vomiting, and weight loss. Commonly, the presence of positive fecal occult blood or of even frank hematochezia is evident. Because patients with ARF often receive renal replacement therapies early in the disease course (or perhaps also because of more frequent exposure to antibiotics), uremic enterocolitis is encountered rarely in clinical practice. Because of the frequent need to use antibiotic therapy combined with the presence of an impaired immune system and the reduction of gastrointestinal motility, patients with ARF suffer from an increased incidence of *Clostridium difficile*–associated pseudomembranous colitis.[68] Although

patients afflicted by this form of colitis usually have severe symptoms, some may be asymptomatic. A high index of suspicion for this serious ailment is required. Its eradication has become more difficult with the emergence of increasingly resistant organisms.

Constipation in ARF patients can result from the administration of aluminum-based antacids, sucralfate, iron, calcium carbonate,[69] or analgesic narcotics, as well as from a restricted fluid intake. During hemodialysis, the splanchnic blood flow is reduced even if blood pressure remains within normal limits.[70] Often transient, this reduction may be more marked and more persistent in patients with hypotension. It has been suggested that episodes of hypotension from any cause (such as those from volume depletion resulting from vomiting, diarrhea, or excessive ultrafiltration) may precipitate bowel infarction.[71] On account of a variety of complicating factors such as old age, chronic hypertension, hyperlipidemia, diabetes, and elevated serum calcium-phosphorus product, many ARF patients suffer from atherosclerosis, arteriosclerosis, and calcification of blood vessels. When these patients experience hypotension, bowel ischemia and infarction can occur as a result of the failure of the damaged mesenteric blood vessels to respond to the hypotension through vasodilatation (failure of autoregulation). Prevention of mesenteric ischemia entails the maintenance of a proper blood volume and the avoidance of hypotension. In cardiovascularly unstable patients requiring renal replacement treatment, the use of techniques that can lessen the precipitation of hypotension such as slow, low-efficiency daily dialysis or CRRTs is preferred. Bowel infarction requires emergency surgery and carries a high morbidity and mortality.

Uremia is a common cause of metabolic ("paralytic") ileus. The ileus is of the overactive or spastic type, and its manifestations are similar to those of mechanical ileus or of intestinal obstruction.[8] Metabolic ileus occurs most frequently in posttraumatic ARF and crush syndrome, in which the ileus often is confused with the primary pathologic features of injury.[8] Thus the decision whether to perform exploratory surgery can be difficult.

In some reports, mucosal injury or necrosis of the large intestines developed in uremic patients after rectal administration of a mixture of sodium polystyrene sulfonate (SPS) and sorbitol.[72] Similar lesions also have been found, albeit less frequently, in the upper gastrointestinal tract after oral administration of the mixture.[73] In severe cases, bowel perforation has occurred. Studies in experimental animals have suggested that sorbitol alone was the culprit in this bowel complication.[72] Similar data for humans are lacking, however. At this stage of incomplete knowledge, it seems prudent to use instead another laxative in the case of oral SPS administration and another liquid vehicle in the case of rectal administration. Finally, SPS, when given orally alone, can bring about fecal impaction, especially in the face of dehydration and in the elderly. Because the serious complication of intestinal necrosis often is associated with a high mortality rate, some authors have suggested that it would seem wise to avoid the use of SPS to treat hyperkalemia, unless such use is absolutely necessary and no other means of treatment are available.

Hepatic Disease

ARF often is associated with the concomitant failure of other organs—that is, multiorgan system failure (MOSF).[74] Hypoxic hepatic injury ("shock liver"), frequently because of hypotension, is seen commonly in this setting. There is usually an early and sometimes transient elevation in serum hepatic enzyme values followed by a steady rise in serum bilirubin levels and frank jaundice. Histologic changes in the liver include centrilobular necrosis, bile stasis, and fatty infiltration.[74] The risk of infection is heightened by a combination of hepatic failure and renal failure. Azotemia is a predisposing factor for hepatic encephalopathy in patients with concomitant liver failure. This predisposition is believed to be due to the absorption of ammonia produced in the gut lumen in quantities much larger than usual because of the increased amount of available urea,[75] as well as to the accumulation of other toxic nitrogenous products. A higher blood pH can bring about a higher NH_3/NH_4^+ ratio, thereby augmenting the transport of the easily diffusible NH_3 across the blood-brain barrier and worsening the encephalopathy.[76] Intermittent modes of renal replacement therapy have been shown to lead to an increase in intracranial pressure and cardiovascular instability in susceptible patients with concomitant acute liver failure and renal failure.[46,77,78] Such changes are the result of a combination of (1) adverse effects on cerebral oxygen delivery or cerebral perfusion pressure, or both[77]; (2) the generation of an osmotic gradient between plasma on the one hand and cerebral and other tissues on the other; and (3) possibly too-rapid removal of excess fluid from the vascular space in a patient in a malnourished and weakened state. With CRRTs, these cardiovascular and cerebrovascular changes generally are much ameliorated.[46,77,78] Patients with hepatic failure are at risk for intracranial hemorrhage. Conventional heparin administration during renal replacement therapies may precipitate bleeding more readily. Consequently, heparin-free or regional citrate administration approaches are preferred.[45,46]

Because of all of the aforementioned concerns, when a patient with combined liver dysfunction and ARF requires renal replacement therapy, the use of an appropriate (commonly lower than normal) bicarbonate level in the dialysis solution or replacement fluid (e.g., 30 mM or lower) to ensure that metabolic alkalosis does not occur, the use of a slightly higher-than-normal sodium level in the dialysis solution or replacement fluid (e.g., greater than 140 mM) to discourage entry of water into the brain during treatment, and the use of a treatment technique that avoids or minimizes bleeding should receive careful consideration.[45,46,79] Because patients with liver dysfunction may not be able to metabolize lactate or citrate readily,[80] it seems prudent to use a bicarbonate-based dialysis or replacement solution for all patients with concomitant hepatic and renal dysfunction and to monitor plasma bicarbonate level often when regional citrate anticoagulation is practiced. Finally, in severe cases of uncontrolled intracranial pressure, cooling of the dialysis or replacement solution may be helpful, in addition to other measures to cool the patient to 32° to 33°C. At these temperatures, oxygen demands of the brain are reduced.[46]

GASTROINTESTINAL TRACT–RELATED ACID-BASE AND ELECTROLYTE DISTURBANCES ASSOCIATED WITH ACUTE RENAL FAILURE

Metabolic alkalosis can develop readily in patients with ARF suffering from vomiting or undergoing nasogastric suction, if the resultant loss of hydrogen ions is greater

than the gain as a result of renal dysfunction. In this clinical setting, the hydrogen cation that is derived from carbonic acid and secreted by the gastric parietal cells along with the chloride anion in the form of hydrochloric acid, is removed from the body, and the bicarbonate anion left behind is retained because of failure of renal excretion. Prophylactic use of H_2 blockers or proton pump inhibitors in patients undergoing nasogastric suction or suffering from vomiting is effective in the prevention of metabolic alkalosis, but such agents will not correct any existing metabolic alkalosis once it has been generated.[69] In the presence of renal failure, any nonprogressing metabolic alkalosis will be corrected gradually by the metabolic acidosis secondary to renal failure (unless the patient receives renal replacement therapy using low buffer-base dialysis solution or replacement fluid for the correction of the metabolic alkalosis).

Administration of excessive quantities of absorbable alkali, such as sodium bicarbonate and calcium carbonate, in patients with renal dysfunction also can result in metabolic alkalosis. Although the use of nonabsorbable antacids in the form of aluminum- or magnesium-containing compounds ordinarily does not cause metabolic alkalosis, combined administration of these agents and sodium polystyrene sulfonate can produce metabolic alkalosis. In patients with ARF, severe metabolic alkalosis can be treated with hemodialysis, peritoneal dialysis, hemofiltration, or hemodiafiltration using buffer base–poor and chloride-rich dialysis solutions, or replacement fluids.[80–82]

Hypernatremia can result from the diarrhea induced by lactulose therapy given for the treatment of hepatic encephalopathy.[83] The administration of sodium phosphate salts as oral laxatives or as enemas is not advised in ARF because of the frequent occurrence of hyperphosphatemia and hypocalcemia.[84] Worsening of renal function also can occur. In its extreme, hyperphosphatemia induced by the administration of sodium phosphate by the foregoing mechanisms can be accompanied by hypernatremia and an increased anion gap in the plasma.[84] On the other hand, at times, hypophosphatemia may develop in certain patients with ARF, as a result of, for example, reduced oral phosphorus intake, excessive phosphate binder ingestion, parenteral nutrition, administration of glucose, or intensive renal replacement therapy.[84] With true phosphate depletion, soluble sodium phosphate salts can be given judiciously by the oral or intravenous route or in the dialysis solution or replacement fluid.[79,84–86]

DRUG-PRESCRIBING GUIDELINES IN ACUTE RENAL FAILURE

The drug-dosing guidelines for drugs that are excreted by the kidney are derived mostly from studies carried out in patients with stable, chronic renal dysfunction. An important point in this regard is that the equations of Cockcroft and Gault,[87] as well as those of the Modification of Diet in Renal Disease (MDRD) study,[88] were derived from data for patients with steady-state chronic renal functional impairment. Therefore, unless the patient with ARF has stable renal function, these equations should not be applied to estimate creatinine clearance (in the case of the Cockcroft-Gault equations) and glomerular filtration rate (in the case of the MDRD equations). Finally, in patients who retain some degree of renal function, cimetidine reduces the secretion of creatinine into the proximal tubule, leading to an elevation in serum creatinine concentration.[89] By contrast, ranitidine has no effect on tubular secretion of creatinine.[90]

With regard to drugs that are metabolized by the liver, an important consideration is that many ARF patients also suffer from concomitant liver dysfunction and therefore also may require a reduction in dosages of such drugs.

Key Points

1. Gastrointestinal bleeding, often the result of stress-related mucosal disease, is still frequently encountered in patients with acute renal failure.
2. Histamine H_2 receptor antagonists and proton pump inhibitors often are used in the prophylaxis and management of gastrointestinal bleeding that is secondary to stress-related mucosal disease.
3. Problems involving other aspects of the alimentary tract in the form of, for example, colonic ulceration, pancreatitis, cholecystitis, liver ailments, and gastrointestinal tract–related acid-base and electrolyte disorders deserve emphasis.

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