A 77-year-old man with symptomatic coronary atherosclerotic heart disease was admitted for elective coronary revascularization. He had a history of chronic obstructive pulmonary disease due to cigarette smoking and essential hypertension. He was managed on diuretics and a salt-poor, low-cholesterol diet. An echocardiogram revealed left ventricular hypokinesis and atrial enlargement. Wide and notched P waves in standard leads II and III of the electrocardiogram were considered to be related to his chronic obstructive pulmonary disease, which put him at risk for postoperative atrial fibrillation (AF). A cardiac consultant advised adding vitamin C (ascorbic acid) to his management.

QUESTIONS

1. Which of the following statements regarding vitamin C is/are correct?
   a. vitamin C deficiency is rare in developed countries
   b. vitamin C deficiency increases mortality
   c. vitamin C deficiency is common in diabetics
   d. vitamin C can be toxic in high doses
   e. in the past, vitamin C was synthesized by humans

2. Which of the following are correct?
   a. atrial fibrillation is an expected, benign postoperative complication
   b. β-blockers are effective in preventing postoperative AF
   c. vitamin C may play a role in preventing postoperative AF
   d. atrial remodeling may be caused by oxidative stress

ANSWERS

1. b. vitamin C deficiency increases mortality
   c. vitamin C deficiency is common in diabetics
   e. in the past, vitamin C was synthesized by humans

Vitamin C (ascorbic acid) is an essential element in the adult population. It is a cofactor in enzymatic functions necessary for metabolic reactions, such as biosynthesis of collagen, amino acids, and norepinephrine. Vitamin C is a powerful antioxidant that protects cellular constituents (proteins, lipids, and DNA) and protects against oxidative stress produced by peroxide and free radicals. Vitamin C is found in fruits and vegetables and synthesized by most living creatures. Humans and the higher primates lost this function millions of years ago and are now dependent on exogenous sources of this essential nutrient. Although scurvy, a disease of severe vitamin C deficiency, is rarely seen in developed nations, prevalence of vitamin C deficiency has been found in the adult population of the United States. Low vitamin C serum concentrations were found in 25% of non–cigarette smoking adult men 60 to 74 years of age. The incidence in the younger population has been less striking, but not insignificant.

Vitamin C requirements increase during trauma or injury, reflecting an increase in vitamin
C utilization and metabolism. Diabetics and cigarette smokers have lower serum levels of vitamin C. Symptomatic of severe vitamin C deficiency (which may precede overt scurvy) include fatigue, weakness, myalgia, irritability, skin rash, and swelling of the lower extremities. Some of these symptoms are vague but physiologically relevant and may be overlooked or misdiagnosed.

Vitamin C is not highly toxic and interacts with a number of medications such as aspirin, nonsteroidal antiinflammatory drugs, aceterminophen, loop diuretics, β-blockers, tetracycline, and cyclosporine; consequently, vitamin C levels should be monitored. Warfarin therapy was thought to be problematic when administered with vitamin C; however, subsequent findings did not support the earlier case reports. Warfarin can be administered with vitamin C at doses not exceeding 1000 mg daily, but requires monitoring of the prothrombin time/international normalized ratio. Additionally, vitamin C reduces the development of nitrate tolerance.

2. c. vitamin C may play a role in preventing postoperative AF
d. atrial remodeling may be caused by oxidative stress

Atrial fibrillation, a common arrhythmia following cardiac surgery, has an incidence of 20% to 30% that is even greater following valvular heart procedures. Atrial fibrillation, which in the past was considered to be a transient and benign arrhythmia, is actually a significant cause of postoperative morbidity and mortality. Postoperative patients in whom AF develops have an increased incidence of strokes and perioperative myocardial infarction, are prone to development of congestive heart failure and respiratory failure, and thus are at an increased risk of mortality. Postoperative AF is a major cause of morbidity and mortality in cardiac surgery and increases the length of stay in the intensive care unit, as well as total hospitalization, by approximately 3 days. In-hospital mortality and long-term mortality (5 years) are also increased.

The pharmacological agents used in the prevention of postoperative AF brought modest results. These include β-blockers, sotalol, and amiodarone. The role of vitamin C was studied in 100 randomized patients undergoing coronary bypass surgery; half received ascorbic acid and a β-blocker preoperatively and postoperatively, and the other half received only a β-blocker. The group that received both vitamin C and a β-blocker had a 4% incidence of AF compared with 25% in the control group. Additional studies have reported similar findings. In a study on the role of vitamin C in the prevention of early recurrence of AF following cardioversion, AF recurred in 4.5% of patients pretreated with vitamin C, compared with 36.3% in the control group. The control group treated with vitamin C had a significant reduction in serum inflammatory indices, such as white blood cell count, fibrinogen level, and level of C-reactive protein.

Many factors have been implicated in the etiology of postoperative AF, including acute intraoperative atrial enlargement, ischemia, surgical trauma, pericarditis, chronic obstructive pulmonary disease, hypertension, hypomagnesemia, inadequate cooling of the atria, and withdrawal of preoperative β-blockers. Inflammation after cardiac surgery is a significant factor in the genesis of AF. Surgical trauma and the ischemic and reperfusion injury that ensues promote the accumulation of proinflammatory cytokines responsible for oxidative stress that in turn are caused by oxygen radical signaling. Surgical trauma also causes a depletion of plasma antioxidants. The inflammatory process affects the electrophysiological properties of atrial myocytes. Experimental evidence correlates oxidative stress with atrial electrical remodeling. The strong antioxidant properties of ascorbic acid are thought to attenuate the impact of oxidative damage, blunt the inflammatory response and atrial remodeling, and thereby lessen the chances for postoperative AF. Finally, the multiple factors that may be implicated in the incidence of postoperative AF can be attenuated by the preoperative and postoperative administration of vitamin C (ascorbic acid).

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The Importance of Vitamin C in the Incidence of Atrial Fibrillation
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