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Hypokalemia and Cardiac Arrhythmias

THE RELATIONSHIP between hypokalemia and cardiac arrhythmias is intriguing, important, and complex. Clinicians have long suspected that hypokalemia favors the development of serious cardiac arrhythmias in patients with ischemic heart disease, digitalis toxicity, or a history of serious cardiac arrhythmias.[1] Standard clinical practice in these patients has been to restore the serum potassium to the normal range. The importance of modest reduction in serum potassium in patients without overt heart disease or arrhythmias remains controversial, however. Standard anesthesiology teaching has recommended delaying elective surgery in patients with serum potassium values below some arbitrary level.[2] Recently, the significance of hypokalemia in the genesis of cardiac arrhythmias has been questioned and has prompted vigorous debate.[1,3] Anesthesiologists have been challenged to enter this fray by an article from Vitez *et al.* in this issue.[4] The authors of this study question the importance of hypokalemia in anesthetized patients. Before addressing this article in detail, I will briefly review the evidence linking hypokalemia and cardiac arrhythmias.

In cellular electrophysiologic studies, hypokalemia has been shown to increase pacemaker discharge rates due to an increase in the slope of phase 4 diastolic depolarization, thus favoring the emergence of automatic rhythms.[5] Hypokalemia has also been demonstrated to cause slowing of conduction, dispersion of refractoriness, and unidirectional block in experimental preparations, thereby providing the substrate for reentrant cardiac arrhythmias to develop.[5] In isolated, perfused rabbit heart preparations, severe (75%) reduction in the concentration of potassium in the perfusate results in spontaneous ventricular fibrillation that can be reversed by increasing the potassium concentration.[6] Lesser degrees of potassium reduction in such models renders the heart more vulnerable to electrically provoked ventricular fibrillation. Surprisingly, adequate *in vivo* animal studies addressing the arrhythmogenic potential of hypokalemia in the presence and absence of myocardial ischemia have not been performed.

Clinical studies have shown consistent alterations in the electrocardiogram with progressive lowering of the serum potassium; the most characteristic changes are a sagging ST-segment, a low T-wave, and a prominent U-wave. Severe hypokalemia (<2.5 mEq/l) has been associated with the development of dangerous ventricular tachyarrhythmias, even in the absence of heart disease or digitalis therapy.[5] Acute lowering of serum potassium may be more arrhythmogenic than chronic hypokalemia.[5] The association between more modest hypokalemia (2.5–3.5 mEq/l) and serious cardiac arrhythmias is less clear and is the focus of the current debate. Hypokalemia resulting from long-term diuretic therapy of hypertension may increase the incidence of ventricular ectopy but has not been shown convincingly to increase the risk of sudden death.[3] Harrington *et al.* pointed out the methodologic flaws in studies purporting to show increased ventricular arrhythmias in moderately hypokalemic patients not treated with digitalis.[3] The hazards, cost, and unproven benefit of potassium repletion also were emphasized by these authors.

Since that analysis appeared in 1982, several studies have raised the spectre of serious cardiovascular risk from hypokalemia in some patients, particularly those with known cardiac abnormalities and especially in the setting of acute myocardial ischemia. The Multiple Risk Factor Intervention Trial group found a higher than expected mortality, mostly sudden death, in a subset of hypertensive patients treated with diuretics who had preexisting electrocardiographic abnormalities.[7] This finding remains unexplained. Hypokalemic mediated arrhythmogenesis is a plausible, but still unproven, hypothesis to account for this observation.

Further data also have been published recently concerning the association of hypokalemia and ventricular

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fibrillation in the setting of acute myocardial infarction.[8] Nordehaug and von der Lippe studied 1,074 patients with acute myocardial infarction, of whom 122 had hypokalemia (<3.5 mEq/l) on admission to the hospital. Primary ventricular fibrillation occurred early in the course of hospitalization in 92 patients. The incidence of ventricular fibrillation was significantly higher among those with hypokalemia compared with patients with normal serum potassium values (17.2% *vs.* 7.5%, $P < 0.01$). In this study, the lower the potassium level, the higher the risk of ventricular fibrillation observed without other apparent explanation for these findings. Thus, eight of 24 patients (33%) with serum potassium levels ≤ 3.0 mEq/l developed primary ventricular fibrillation. The mean time from admission to the development of ventricular fibrillation was less than 30 min in the hypokalemic group, suggesting that hypokalemia may favor the development of ventricular fibrillation early in the course of acute myocardial infarction or with prolonged ischemia. These and other data have reinforced clinicians' fears that hypokalemia in patients with known or suspected cardiac disease increases the risk of serious ventricular arrhythmias, especially in the setting of myocardial ischemia.

What is the relevance of these observations to the practice of anesthesiologists? Fortunately, serious ventricular arrhythmias and cardiac arrest are rare during the perioperative period in most groups of patients.[9] Perioperative myocardial ischemia, ventricular arrhythmias, and cardiac death are most common in patients with preexisting cardiac abnormalities.[10,11] In particular, recent myocardial infarction, congestive heart failure, cardiac arrhythmias, and aortic stenosis have been identified as independent determinants of risk of perioperative cardiac complications, including serious ventricular arrhythmias.[11] Other important factors include the age and general medical condition of the patient, as well as the nature of the surgery being performed. Cardiac surgery, needless to say, is particularly associated with arrhythmias, but other intrathoracic, intraperitoneal, and aortic operations also have been identified as being determinants of cardiac risk.[11-13] It is in these groups of patients, therefore, that hypokalemia may be of particular importance. Until now, no studies have specifically addressed the relationship between serum potassium and perioperative cardiac arrhythmias. Although Goldman *et al.* did include hypokalemia as one element in "poor medical condition" that correlated with increased perioperative cardiac risk, hypokalemia was not independently analyzed, and no data were provided to substantiate the association.[11]

In this issue, Vitez *et al.* report that moderate hypokalemia (<3.5 mEq/l) did not increase the incidence of intraoperative arrhythmias in their patients. In this study, a serum potassium determination was obtained within 24 h before anesthesia. Heart rhythm was monitored by Holter® monitor or by a trained observer. Patients were divided according to the preoperative potassium determination, those patients with serum potassium values below 3.5 mEq/l being considered hypokalemic. No patient developed serious cardiac arrhythmias, and there was no difference between the groups in the incidence of minor rhythm disturbances. Based on these results, Vitez *et al.* challenge the practice of postponing surgery and repleting potassium in patients found to have a low serum potassium value.

Several aspects of this study require emphasis. The study population appeared to be at low risk of serious arrhythmias; the great majority of patients had no known cardiac disease, were not taking digitalis, and had only modest reduction in serum potassium. In the hypokalemic group, only 21 of 62 patients had serum potassium levels less than 3.0 mEq/l, and no patient had a level below 2.6 mEq/l. Some patients in the hypokalemic group may not have been hypokalemic at the time of anesthesia, as low initial serum potassium levels tend to rise in patients admitted to hospital whether or not potassium replacement therapy is given.[14] In the hypokalemic group of patients, most operations appeared to be minor, or at least not those specifically associated with a high incidence of cardiac complications. For those reasons, the expected incidence of serious arrhythmias in Vitez's study would be very low indeed, as was the case. This study could not detect a difference in serious arrhythmias between groups unless that difference was very great. Benign arrhythmias occurred with equal frequency in both groups. It could be argued that even if hypokalemia increased the incidence or frequency of ventricular or atrial premature beats, this could not be of clinical importance, since these arrhythmias are only of prognostic significance in patients with cardiac disease.[15] The data of Vitez *et al.* cannot be applied to higher risk populations as defined earlier. As the authors indicate, they did not monitor their patients postoperatively, therefore, these results cannot be applied to that situation.

These reservations should not detract from the important issues raised by Vitez *et al.* In patients at low risk of cardiac complications of surgery and anesthesia, modest reduction in serum potassium (3.0–3.5 mEq/l) should not prompt postponement of surgery and acute potassium repletion. In patients with more severe potassium depletion and in higher risk groups, however, there are no data in this study to prompt a change in current practice. Anesthesiologists must consider the significance of an individual serum potassium determination in accordance with the clinical setting in which it was measured. Further experimental and clinical

studies are clearly needed to assess the arrhythmogenic potential of modest potassium depletion, especially in the setting of myocardial ischemia with and without concomitant digitalis therapy. The influence of perioperative catecholamine release on potassium homeostasis and myocardial ischemia warrants investigation also.[16] Until such studies are performed, it is prudent to consider even modest hypokalemia (<3.5 mEq/l) undesirable in patients at increased risk of perioperative cardiac complications.

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