Drug-Induced Hypokalaemia
A Cause for Concern

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Summary

Drug-induced hypokalaemia is a widespread problem in the elderly that can be caused by many therapeutically useful substances, the most common of which are diuretics. In certain classes of patients (e.g. those with acute myocardial infarction, with congestive heart failure receiving digitalis, or with cirrhosis), iatrogenic hypokalaemia is an established risk factor. In patients with hypertension who have no underlying heart disease or liver disease, the use of diuretics may lead to worsened glucose tolerance and cardiac arrhythmias. There is also evidence for an increased risk of sudden cardiac death.
A number of clinical manifestations may accompany potassium depletion (Holland 1984; Nar­done et al. 1978). Though potassium depletion can lead to muscle cramps and other symptoms, the monitoring of potassium status in the elderly by symptomatology is fraught with difficulty because they are relatively less likely to have classic symp­toms (since they are less active) and their symp­toms may be confused with other medical prob­lems. Therefore, serum potassium determinations are relatively more important in assessing their po­tassium status. The elderly are particularly at risk of some of these manifestations since they may be predisposed to becoming potassium depleted: they may be less likely to have an adequate dietary in­take of potassium, they may be on a greater num­ber of medications that might lead to potassium depletion, and the medications that they take may be relatively more potent as a result of decreased metabolic clearance rate and decreased binding by plasma proteins, which favours drug delivery to target tissues. Furthermore, the elderly commonly receive diuretics, for a variety of reasons. Thus, consideration of a number of manifestations of po­tassium depletion that may result from drug therapy in the elderly is important in the clinical care of these individuals.

Hypokalaemia, defined as a serum potassium level of less than 3.5 mmol/L, is an extremely common clinical problem. Prevalence estimates vary according to the population studied. Among hos­titalised patients in general, one large study found the frequency to be 21% (Paice et al. 1986). It is estimated that 2% of healthy adults have hypokalaemia (Knochel 1984), while potassium levels of less than 3.5 mmol/L will develop in 30 to 50% of diuretic-treated patients (Gifford 1976).

Mild hypokalemia is common. One study found serum potassium levels of less than 3.0 mmol/L in 5% of patients (Paice et al. 1986). Severe, life-threatening hypokalaemia, defined as a serum po­tassium level of less than 2.5 mmol/L, is very rare. A review of 13 years of data at an Israeli hospital showed an incidence of only 0.03% (Halevy et al. 1988). Of those cases, 68% were the result of drug therapy.

1. Adverse Effects of Hypokalaemia

1.1 Cardiac Effects

Although there is little controversy about the adverse cardiac effects of potassium levels less than 2.5 mmol/L the adverse effects of mild hypokalaem­ia have remained an area of research and debate. Severe hypokalaemia induces a number of electrocardiographic abnormalities (table I). Flattening of the T wave is an early sign, with the appearance of a U wave and a depressed ST segment being present in more severe cases. Hypokalaemia predisposes affected persons to ventricular fibril­lation and ventricular tachycardia by increasing the relative refractory period and thus the chance of a re-entry mechanism arrhythmia. The magnitude of the danger of mild hypokalaemia is unclear. One study (Multiple Risk Factor Intervention Trial Re­search Group 1982) showed an increased risk of sudden cardiac death in presumably potassium­depleted patients treated with diuretics. Some studies were able to show an increased risk of ventricular arrhythmias with diuretic-induced hypo­kalaemia (Holland et al. 1981, 1988; Hollifield & Slaton 1981), whereas others have not (Madias et al. 1984; Papademetriou et al. 1988). The latter studies have suffered from several factors that lim­ited their ability to identify diuretic-induced ven­tricular arrhythmias (Holland 1986). In general, however, patients with acute myocardial infarction have an increased risk of ventricular tachycardia which is almost linearly related to the degree of hypokalaemia (Nordrehaug et al. 1985). Patients treated with antiarrhythmic agents are at risk of

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