Serum potassium concentration as a risk factor of ventricular arrhythmias early in acute myocardial infarction

Jan Erik Nordrehaug, M.D., Karl-Arne Johanesen, M.D., and Gerhard von der Lippe, M.D., Ph.D.

ABSTRACT Sixty patients with a first acute myocardial infarction and no current treatment with cardiovascular drugs were included in a prospective study of the relationship between serum potassium concentration and the early occurrence of ventricular tachycardia and premature ventricular contractions (PVCs). Serum potassium level (range 2.5 to 5 mmol/liter) was estimated 3.8 ± 2.5 hr (mean ± SD) after the onset of the infarction, and Holter monitoring was performed during the subsequent 12 hr. In multivariate analysis, serum potassium level was negatively and age positively related to ventricular tachycardia. Among the subclasses of PVCs (frequent unifocal, multifocal, couplets, bigeminy), serum potassium concentration was negatively related to the frequent unifocal subclass; hypertension was related to couplets and to the presence of any of the subclasses, and serum aspartate aminotransferase concentration was related to multifocal PVCs. Heart failure leading to death was related to all subclasses of PVC. Serum potassium concentration is an independent inverse predictor of the occurrence of ventricular tachycardia and frequent unifocal PVCs early in acute myocardial infarction.


LOW CONCENTRATIONS of serum potassium or serum magnesium on admission to the hospital have been associated with an increased occurrence of ventricular arrhythmias in patients with acute myocardial infarction.1–4 This association has been shown for ventricular arrhythmias occurring around the time of hospital admission1,5 rather than later during the infarction.1,4,6 However, the patients have been grouped according to arbitrary points between low and normal electrolyte levels, or they have been divided into subgroups based on electrolyte measurements organized into arbitrary ranges of measured values. None of the studies has assessed the relative importance of serum potassium and magnesium concentrations for arrhythmias. Other variables that may influence the frequency of arrhythmias have often not been reported, and treatment with digitalis may have confounded the relationship between electrolytes and arrhythmias.

This prospective study was undertaken to examine serum potassium and serum magnesium levels as continuous variables and to evaluate their relationship to early ventricular arrhythmias in patients with acute myocardial infarction. Statistical analysis with stepwise logistic regression to select predictor variables for the arrhythmias was used to overcome some of the previous limitations of assessing the relationship of these electrolytes with arrhythmias.

Patients and methods

This was a prospective study of 60 patients admitted to our coronary care unit within 12 hr of the onset of symptoms of a first acute myocardial infarction. The patients gave informed consent to participate in the study. The diagnosis was based on the presence of at least two of the following: chest pain typical of myocardial infarction of more than 30 min duration, recent ST segment elevation followed by T wave inversion, or the development of Q waves in the electrocardiogram with no evidence of prior myocardial infarction, and the transient elevation of two separate serum aspartate aminotransferase values above the upper limit of normal.7 Exclusion criteria from the study included current treatment with digitalis, β-blockers, calcium antagonists, or antiarrhythmic drugs; cardiogenic shock; alcoholism; atrioventricular block greater than grade 1; or bundle branch block in the electrocardiogram.

All patients were admitted to the unit and were treated with oral diazepam, oxygen, and morphine in the acute phase. No patients were given potassium or magnesium supplements, prophylactic antiarrhythmic agents, or anticoagulants. Heart failure was defined as previously described8 and was treated exclusively with furosemide. One patient had ventricular fibrillation (6 hr after hospital admission), and only this patient received antiarrhythmic therapy. No other cardiovascular drugs were used in any patient during the study period.

Blood samples for the estimation of serum potassium and magnesium concentrations were taken on admission to the hospital and centrifuged immediately. The blood was taken from a cubital vein with the arm at complete rest. Serum potassium level was analyzed by flame photometry and serum magnesium level by atomic absorption spectroscopy.

Electrocardiographic QT intervals were measured in standard lead II in a 12-lead electrocardiogram taken on admission to the hospital. The QT intervals were measured by the authors without the knowledge of the serum potassium or magnesium val-
ues. Interobserver differences were small, and when differences existed the mean values were used. Corrected QT intervals were calculated according to the formula QT/\(R-R\) interval.

**Detection of ventricular arrhythmias.** In all patients, continuous recordings of the electrocardiogram were made with an Avionics model 445 two-channel tape recorder for the first 12 hr after the admission. The recordings were analyzed beat-to-beat from the paper printouts of a two-channel Avionics Vis-U-Scan model 9200. All the paper printouts were read by visual counting by the authors, without prior knowledge of serum potassium or magnesium concentrations or the clinical characteristics of the patients. Arrhythmias were interpreted at a paper speed of 25 mm/sec or faster when necessary for accurate interpretation. All printouts had more than 11 analyzable hours. The interobserver differences in noting the presence or absence of the various classes or subclasses of ventricular arrhythmias were small (<5%).

The arrhythmias considered for study were: (1) ventricular tachycardia, defined as three or more consecutive ventricular complexes at a rate of greater than 120 beats/min, and (2) premature ventricular contractions (PVCs), subclassed as frequent (>5 isolated unifocal beats/min), bigeminy (alternate sinus and ventricular beats), multifocal (multifocal beats in the same hour of recording), couplets (two consecutive ventricular beats, R-on-T—according to R-\(R\)-R-\(T\) <0.85), and overall frequency (total number of PVCs in the recording divided by the number of analyzable hours and expressed as the number per hour).

**Statistical analysis.** All tests presented in this report were two-tailed; p values below .05 were considered significant. Stepwise logistic regression (BMDP statistical software) was used when the dependent variable (arrhythmia) was a dichotomy. Stepwise regression was used to analyze the relationship between the various independent variables and the total number of PVCs. Linear regression analysis was used to correlate serum potassium and serum magnesium concentrations.

**Results**

Values are expressed as mean ± SD. The various ventricular arrhythmias are analyzed in the tables and figures as “present” or “absent” in each patient. The number of hours from the onset of symptoms of infarction to hospital admission for the total of 60 patients (54 men) was 3.8 ± 2.5. The mean age was 66.1 ± 9.7 years. Twenty-six patients had anterior wall infarction and 29 inferior wall; five had infarction of uncertain location. The mean peak serum aspartate aminotransferase level was 246 ± 135 U/liter (4.108 ± 2.255 \(\mu\)kat/liter). The mean serum potassium and magnesium levels were 3.86 ± 0.56 and 0.76 ± 0.09 mmol/liter, respectively. There was no relationship between serum potassium and serum magnesium concentrations (r = .16, n = 60, NS).

Table 1 shows the demographic and clinical characteristics of the patients analyzed as continuous or discrete variables as appropriate to select those with a significant relationship to ventricular tachycardia. This arrhythmia was inversely related to serum potassium and magnesium concentrations and was related to hypertension and cardiomegaly by univariate analysis.

**Multivariate analysis** identified serum potassium level as an inverse predictor and age as a predictor of ventricular tachycardia. There was no significant interaction between serum potassium level and age.

The episodes of ventricular tachycardia were self-limiting in all cases, including patients with more than one episode of this arrhythmia. Eighteen patients had ventricular tachycardia; the number of beats in each episode (range 3 to 23) was 3 in three patients, between 4 and 10 in seven patients, and more than 10 in eight patients.

Of the 19 patients treated for hypertension (table 1), 17 were currently receiving thiazides, and two were taking no diuretic drugs. Nineteen of the 20 patients treated with diuretics before admission (table 1) had

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of patients</th>
<th>Univariate analysis (p value)</th>
<th>Summary multivariate analysis (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (range 49 to 84 yr)</td>
<td>60</td>
<td>.07</td>
<td>.036†</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td>.46</td>
<td></td>
</tr>
<tr>
<td>Hours from onset of symptoms to admission (range 0.5 to 11)</td>
<td></td>
<td>.24</td>
<td></td>
</tr>
<tr>
<td>Clinical history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated hypertension</td>
<td>19</td>
<td>.047†</td>
<td></td>
</tr>
<tr>
<td>Diuretic treatment</td>
<td>20</td>
<td>.24</td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td>24</td>
<td>.31</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>23</td>
<td>.53</td>
<td></td>
</tr>
<tr>
<td>Serum potassium (range 2.5 to 5 mmol/l)</td>
<td></td>
<td>.016†</td>
<td>.016†</td>
</tr>
<tr>
<td>Serum magnesium (range 0.57 to 0.92 mmol/l)</td>
<td></td>
<td>.048†</td>
<td></td>
</tr>
<tr>
<td>Initial heart rate (range 52 to 139 bpm)</td>
<td></td>
<td>.26</td>
<td></td>
</tr>
<tr>
<td>Infarct location</td>
<td></td>
<td>.76</td>
<td></td>
</tr>
<tr>
<td>Pathologic Q wave in the ECG</td>
<td>39</td>
<td>.86</td>
<td></td>
</tr>
<tr>
<td>Corrected QT interval in the ECG (range 0.32 to 0.53 sec)</td>
<td></td>
<td>.12</td>
<td></td>
</tr>
<tr>
<td>Treatment with furosemide During the first week</td>
<td>21</td>
<td>.32</td>
<td></td>
</tr>
<tr>
<td>Mean daily dosage first week (range 0 to 120 mg)</td>
<td></td>
<td>.89</td>
<td></td>
</tr>
<tr>
<td>During the first 12 hr</td>
<td>9</td>
<td>.82</td>
<td></td>
</tr>
<tr>
<td>Peak aspartate aminotransferase (range 62 to 680 U/l) (1.0354 to 11.356 (\mu)kat/l)</td>
<td></td>
<td>.50</td>
<td></td>
</tr>
<tr>
<td>X-ray film findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>9</td>
<td>.02†</td>
<td></td>
</tr>
<tr>
<td>Lung congestion</td>
<td>6</td>
<td>.07</td>
<td></td>
</tr>
<tr>
<td>Death from heart failure†</td>
<td>7</td>
<td>.44</td>
<td></td>
</tr>
</tbody>
</table>

†Statistical significance.

‡Three patients died before x-ray was taken.

†Total death during hospitalization.
been treated with thiazides. The mean daily dosage of furosemide during the first week (table 1) was 41.4 ± 25.9 mg (n = 21).

Seven patients died in heart failure (table 1), and there were no other deaths during the hospital stay. Two deaths occurred within 24 hr of admission, and the others occurred between 4 and 10 days after admission. Only two of the patients who died of heart failure had evidence of this during the 12 hr monitoring for arrhythmias, and one died within 24 hr of admission.

Figure 1 shows the predicted probability of ventricular tachycardia at the various serum potassium levels. The lowest probability of ventricular tachycardia (0.10 to 0.22) was found at serum potassium levels above 4 mmol/liter; below this there was a steady rise to the highest probability (0.68) at serum potassium 2.5 mmol/liter. Figure 2 shows the individual serum potassium concentrations for patients with and without ventricular tachycardia.

**TABLE 2**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequent unifocal (n = 21)</th>
<th>Multifocal (n = 19)</th>
<th>Couplets (n = 26)</th>
<th>Bigeminy (n = 19)</th>
<th>Any of the preceding subclasses (n = 34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from heart failure</td>
<td>.036</td>
<td>.001</td>
<td>.028</td>
<td>.021</td>
<td>.006</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum aspartate aminotransferase</td>
<td></td>
<td>.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum potassium</td>
<td></td>
<td></td>
<td>.019</td>
<td>.001</td>
<td></td>
</tr>
</tbody>
</table>

*Data are p values from summary stepwise multivariate analysis.*

The variables shown in table 1 were analyzed to determine the relationships to the subclasses of PVCs and to the presence or absence of any of the subclasses. In the univariate analysis, diuretics, hypertension, corrected QT interval, and death from heart failure were related to the presence or absence of any of the subclasses of PVCs. Table 2 shows the p values of the summary multivariate analysis. All the subclasses of PVCs were significantly related to death from heart failure; only frequent unifocal PVCs were related to serum potassium level, and none of the subclasses was related to serum magnesium. R-on-T in the electrocardiogram was observed in only three (5%) of the 60 patients and was therefore not included as a dependent variable in the statistical analysis. Only two patients had diabetes, and this condition was therefore not in-
cluded among the variables shown in table 1. None of the study variables was related to the total number of PVCs.

Discussion

In studies on potassium and arrhythmias in acute myocardial infarction, patients are often divided into hypokalemic and normokalemic groups. Such analysis can disguise much of the information in the data. Further division into subgroups of ranges of the measured potassium values have therefore been done, but this still entails subjectivity in the choice of points that define the ordered categorical subgroups and makes comparison between reports difficult. The use of serum potassium level as a continuous variable in a stepwise logistic regression analysis overcomes these problems and also assesses the relative importance of potassium vs other variables predictive of the arrhythmia in question.

It is most likely for these reasons that the results of the present study differ from previous observations. Both serum potassium and serum magnesium concentrations have been shown to be negatively and the severity of the infarction positively related to the incidence of ventricular tachycardia. This study shows that serum potassium concentration and age were the only independent predictor variables for this arrhythmia.

Low serum potassium values are associated with electrical instability. Our result is therefore in keeping with previous findings that the occurrence of ventricular arrhythmias during the early hours of acute myocardial infarction is related to electrical instability rather than to a bad left ventricular function. In this study, serum potassium level estimated a mean of 3.8 hr after the onset of infarction was associated with ventricular tachycardia. In one study that failed to show an association of serum potassium level with ventricular tachycardia, potassium concentrations were estimated an average of 8 hr after the onset of infarction. Serum potassium concentration is influenced by the catecholamine levels, which are elevated early in acute myocardial infarction, and an acute transient hypokalemic syndrome has been described in patients admitted to the hospital with an acute illness. Thus, in view of such rapid changes in potassium and magnesium concentrations, the relative importance of the relationships among the variables and the arrhythmias may differ according to the stage of the infarct evolution.

Age and cardiac arrhythmias are positively correlated, but a previous report failed to show a relationship between age and ventricular tachycardia. Although few studies have dealt with age in connection with arrhythmias, several reports relate age to a worsened prognosis of patients with acute myocardial infarction, which again is in keeping with an increased occurrence of arrhythmias such as ventricular tachycardia.

Among the subclasses of PVCs, only frequent unifocal PVCs were related to serum potassium level (table 2). Death from heart failure was significantly related to all subclasses of PVCs and to the presence or absence of any of the subclasses, whereas heart failure was not. This difference could be due to the presumably more severe myocardial injury in the patients who died. The results from the analysis of the subclasses of PVCs therefore seem to differ from those of the analysis of ventricular tachycardia. Whereas early ventricular tachycardia and frequent unifocal PVCs may be related to electrical instability that is independent of the degree of myocardial injury, the other subclasses of PVCs may be more closely associated with extensive myocardial injury. An association between complex PVCs and extensive myocardial injury has been suggested in previous reports.

Hypertension was related to subclasses of PVCs. This is more likely to have been due to hypertensive cardiac disease than to side effects of drug treatment, since diuretics, which were the most commonly used antihypertensive agents, were not associated with the occurrence of PVCs.

The clinical relevance of the observed relationship between serum potassium concentration and ventricular tachycardia and frequent unifocal PVCs remains to be determined. The purpose of our study was to relate serum potassium level among other variables to ventricular arrhythmias. However, other studies have related ventricular arrhythmias detected in the acute phase of myocardial infarction to a worsened prognosis of the patients. In a study of 1074 patients with acute myocardial infarction, low (as compared with normal) serum potassium levels on admission to hospital were linked with an increased occurrence of ventricular fibrillation but not with an increased 3 month mortality. Our results confirm that low serum potassium levels are associated with electrical instability. Even though this does not appear to alter the prognosis of hospitalized patients, the role of serum potassium vs electrical instability and sudden death in the prehospital phase of acute myocardial infarction needs to be clarified.

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References

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