

Association of Hypokalemia with Severe Arrhythmias in Patients with Acute Myocardial Infarction

Taysir S Garadah, MD* Salah Kassab, MD, PhD** Jamal Golbahar, PhD***

Background: Clinical and animal studies suggest that the ischemic heart can be particularly vulnerable to hypokalemia leading to the cardiac arrhythmia.

Objective: To evaluate the association of severe arrhythmia with hypokalemia in patients with acute myocardial infarction (AMI).

Design: Retrospective study.

Setting: Coronary Care Unit, Salmaniya Medical Complex.

Method: Two hundred and seventy-four patients with AMI had serum potassium levels measured on admission along with other cardiovascular risk factors.

Result: Serum potassium concentrations were significantly decreased with the severity of arrhythmias (no arrhythmias; 4.2 ± 0.80 mmol/l, supra-ventricular; 3.8 ± 0.9 mmol/l, and ventricular arrhythmias; 3.3 ± 0.5 mmol/l, $p=0.0001$). The risks of supra-ventricular and ventricular arrhythmias were significantly increased by 2.4 and 8.3 fold, respectively in patients with serum potassium levels at the lowest quartile (<3.5 mmol/l) compared with the highest quartile of serum potassium when adjusted for other risk factors.

Conclusion: The results of this study suggest that hypokalemia is independently associated with the severity of arrhythmias in patients with AMI.

Bahrain Med Bull 2011; 33(1):

* Consultant, Cardiac Unit
Salmaniya Medical Complex

** Professor of Physiology
Royal College of Surgeons of Ireland
Medical University of Bahrain

*** Associate Professor
Metabolic and Molecular Diagnostic Unit
Princess Al-Jawhara Centre for Genetic Diagnosis and Research
Department of Molecular Medicine
College of Medicine and Medical Sciences
Arabian Gulf University, Kingdom of Bahrain
Email: Jamalgo@agu.edu.bh

Different electrolytes such as potassium and sodium play an important role in the cell metabolism, electrical conduction and membrane excitability. Abnormalities of these electrolytes due to different causes can lead to a significant cardiac life threatening events.

The cardiac impulse originates in the sinus node distributed into the myocardial cell via the AV node and Bundle of His.

Cardiac rhythm abnormalities can be due to defect in the impulse generation or abnormal conduction or both and can lead to life threatening condition causing low cardiac output and oxygen insufficiency¹.

Studies suggest that arrhythmias are a common clinical feature in cardiac related abnormalities such as coronary artery atherosclerosis, cardiac failure and diabetic cardiomyopathy. Clinical and animal studies suggest that cardiac arrhythmias and conduction abnormalities can cause complications and death during AMI²⁻⁵. Arrhythmias in critically ill patients often have underlying disorders that precipitate their development including hypokalemia, hypomagnesemia, anti-arrhythmic proarrhythmias and myocardial ischemia. While the use of anti arrhythmic drugs and defibrillator to treat life threatening arrhythmia, the correction of electrolyte imbalance remains the mainstay in such clinical condition.

Acute myocardial infarction has been a major clinical problem in the Middle East and Arabian Peninsula causing higher mortalities in Qatar and Saudi Arabia⁶⁻⁷. Severe or fatal arrhythmias such as ventricular fibrillation and ventricular tachycardia are common clinical features in AMI and cardiac failure and are frequent complications in the first 6 hours post AMI and it can directly lead to death if they are not managed promptly^{3,8}. Other supra-ventricular and non-fatal arrhythmias such as atrial fibrillation and supra-ventricular tachycardia are also common in AMI patients⁹.

Clinical and animal studies suggest that the ischemic heart can be particularly vulnerable to hypokalemia; therefore, it is at risk for developing arrhythmias¹⁰⁻¹³. In animal studies, the adverse association between hypokalemia and arrhythmias is reported to be more significant in the presence of AMI¹⁴⁻¹⁷. In clinical studies electrolyte imbalance in patients presenting with AMI has been reported and there are a number of reports suggesting that patients with AMI and hypokalemia on hospital admission can develop ventricular tachycardia or fibrillation and suggest 7-25% prevalence of hypokalemia (defined as <3.5 mmol/L) in patients with AMI¹⁸⁻²⁴.

Although there are many studies suggesting the association of hypokalemia with arrhythmias or a specific type of arrhythmias, there are limited or no studies reporting the association of hypokalemia with the severity of arrhythmias in AMI patients.

The aim of this study is to test the hypothesis that hypokalemia is associated with the severity of the arrhythmias in AMI patients independent of other risk factors.

METHOD

Two hundred and seventy-four consecutive AMI patients were identified from the records of cardiology outpatient department and the Coronary Care Unit from January 2007 to the end of December 2007. Criteria for sustained AMI were the following: cardiac pain more than 20 minutes duration, of less than 6 hours onset and the appearance of new Q wave with ST segment elevation or ST segment depression with more than two fold increase of total creatine kinase (CK).

Patients with normal CK and CK-MB, with recent cardiac surgery in the last 4 weeks, or with history of severe heart failure, cardiogenic shock or severe pulmonary edema and with history of arrhythmias or those with the history of drug overdose on admission were excluded.

All recorded data including past medical history, current-smoking habits, body mass index (BMI), blood pressure, lipid profiles, serum potassium, total CK and CK-MB levels and the use of different medications before (β -blocker blockers and diuretics) and after admission (thrombolytic) were recorded. Subjects were considered hypertensive on admission with a systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg.

Arrhythmias that developed and diagnosed in the first 6 hours from the time of admission were classified into two groups, supra-ventricular arrhythmias (including; atrial fibrillation and supra-ventricular tachycardia) and ventricular arrhythmias (including ventricular tachycardia and ventricular fibrillation).

On the 12 leads ECG, atrial fibrillation was characterized by the replacement of consistent P waves by rapid oscillations or fibrillatory waves that vary in amplitude, shape, and timing, associated with an irregular, frequently rapid ventricular response. The heart rate ranged from 100 to 175 beats a minute. Atrial flutter was characterized by a saw-tooth pattern of regular atrial activation on the ECG, particularly visible in leads II, III, aVF, and V₁.

Supra-ventricular tachycardia was defined as rapid, regular, narrow complex tachycardia of >140 beat per minutes and the ventricular tachycardia was distinguished from supra-ventricular tachycardia with aberrancy by the presence of retrograde P wave activity. Single premature atrial or ventricular ectopic beats were not considered as significant arrhythmia. If one single episode of arrhythmia of similar origin occurred more frequent in the first 6 hours after admission, it was considered and counted as one episode.

Ventricular tachycardia was defined as three or more consecutive ventricular beats in rapid succession at rate of between 120 and 250 beats per minutes seen on a telemetry rhythm strip (non sustained of less than 30 seconds and sustained if more than 30 seconds). Ventricular fibrillation was defined as irregular, rapid, non-coherent ECG activity associated with hemodynamic collapse. The diagnosis was made by two cardiologists using real-time oscilloscope monitoring rhythm strips and 12 leads ECG for all patients.

Serum lipids, creatine kinase were determined with enzymatic photometry and serum potassium levels were measured by flame photometry.

This study complies with the Declaration of Helsinki, and research protocol; it was approved by the locally appointed ethics committee.

Statistical Analysis

The statistical analysis was performed using SPSS (version 17) Software. ANOVA was used for statistical analysis between different groups.

In order to determine the effect of serum potassium on the overall risk and severity of arrhythmias the quartile of serum potassium in those patients without arrhythmias were stratified in quartiles (Q1=<3.5 mmol/l, Q2=3.5-4.2 mmol/l, Q3=4.3-5.1 mmol/l and Q4=>5.1 mmol/l). Serum potassium <3.5 mmol/l was considered hypokalemia.

Stepwise multiple regression analysis was used in order to determine the odd ratio of different level of serum potassium (quartile) on the overall risk and severity of arrhythmia with adjustment for other confounding factors. The quartile of serum potassium in patients were stratified in quartiles (Q1=<3.5 mmol/l, Q2=3.5-4.2 mmol/l, Q3=4.3-5.1 mmol/l and Q4=>5.1 mmol/l).

RESULT

Biochemical and biometric characteristics of patients without arrhythmias and patients with arrhythmias are shown in Table 1. Among the 274 with AMI patients, 84 (30.7%) had admission serum potassium values <3.5 mmol/l. The incidence of hypokalemia was significantly higher in patients with arrhythmias compared to those without arrhythmias, 61 of 130 (46.9%) in patients with arrhythmias compared to 23 of 144 (15.1%) without arrhythmias, $p < 0.01$). In addition, the incidence of hypokalemia of <3.5 mmol/l significantly increased with the severity of arrhythmias, 23 out of 144 (15.9%) in patients with no arrhythmias, 20 out of 64 (31%) in patients with supra-ventricular arrhythmias and 41 out of 66 (62.1%) in patients with ventricular arrhythmias; $p < 0.001$.

Table 1: Biometric and Biochemical Characteristics of AMI Patients with Arrhythmias and Without Arrhythmias

Characteristics	Without Arrhythmias (n=144)	With Arrhythmias (n=130)	<i>p value</i>
Age	58.6 ± 15.5	58.4 ± 17.0	0.50
Gender Male	98 (68%)	77 (59.1%)	0.63
BMI (kg/m ²)	26.4 ± 3.8	26.4 ± 3.6	0.81
Potassium (mmol/l)	4.2 ± 0.8	3.6 ± 0.7	0.001
β-Blockers medication	85 (59.5%)	58 (44.9%)	0.01
Diuretics medication	57 (40.3%)	61 (47.5%)	0.14
Hypertension	79 (55.0%)	80 (62.1%)	0.45
Smoking	86 (60.8%)	74 (57.3%)	0.06

Patients without arrhythmias and on β -blocker were more than 85 of 144 (59.5%) compared to those with arrhythmias 58 of 130 (44.9%, $p<0.010$).

The percentage of patients on diuretic therapy was not significantly different between patients with arrhythmias compared to patients without (44.9%, $p<0.010$).

The incidence of arrhythmias was not significantly different in patients on thrombolytic therapy compared to those not on it. Serum potassium concentration was also not significantly different in patients on thrombolytic drugs compared with those who are not on it (3.9 ± 0.64 verses 3.7 ± 0.90 mmol/l, $p=0.08$).

The biometric and biochemical characteristics of patients categorized according to the severity of arrhythmias are shown in Table 2. Serum potassium was decreased as the severity of arrhythmias increased. The percentage of patients on β -blocker decreased as the severity of arrhythmias increased.

Table 2: Biometric and Biochemical Characteristics According to the Severity of Arrhythmias

Characteristics	Severity of Arrhythmias			ANOVA <i>P value</i>
	Without Arrhythmias (n=144)	Supra-Ventricular (n=64)	Ventricular (n=66)	
Age	58.6 \pm 15.5	58.0 \pm 15.6	58.9 \pm 18.4	0.829
Gender Male (%)	98 (68%)	40 (62.3%)	37 (55.8%)	0.582
BMI (kg/m ²)	26.4 \pm 3.8	26.5 \pm 3.86	26.2 \pm 3.39	0.859
Potassium (mmol/l)	4.2 \pm 0.8	3.8 \pm 0.9	3.3 \pm 0.5	0.0001
Hypokalemia	23 (15.9%)	20 (31.3%)	41 (62.1%)	0.001
β -blockers	85 (59.5%)	23 (35.8%)	36 (54.1%)	0.007
Diuretics	57 (10.1%)	32 (50.9%)	29 (44.1%)	0.625
Thrombolytics	94 (55.4%)	32 (50.9%)	31 (47.1%)	0.816
Hypertension	79 (55.0%)	42 (65.4%)	39 (58.8%)	0.421
Smoking	86 (60.8%)	33 (52.8%)	41 (61.8%)	0.333

In tables 3 and 4 multiple logistic regression analysis indicates that there was 4.7 fold increase risk of arrhythmias with hypokalemia. The risks of supra-ventricular and ventricular arrhythmias were increased by 2.4 and 8.3 folds, respectively, in patients with serum potassium levels at the lowest quartile compared with those with the highest quartile when adjusted for confounding risk factors such as history of hypertension, age, gender, smoking, BMI and diuretics, thrombolytic and β -blocker therapy.

Table 3: Risk of Arrhythmias Associated with Hypokalemia

Quartiles of Serum K (mmol/l)	Cases with arrhythmias (n=130)	Controls without arrhythmias (n=144)	OR (95% CI)	P value
Q1 <3.5 (n=84)	61	23	4.7 (2.5 to 8.7)*	<0.001
Q2 3.5 - 4.2 (n=95)	45	50	0.81 (0.5 to 1.4)*	0.01
Q3 4.3 - 5.1 (n=51)	18	33	0.57 (0.3 to 1.12)*	0.01
Q4 >5.1 (n=44)	6	38	0.31 (0.21 to 0.87)*	0.09

*Adjusted for obesity, hypertension, gender, smoking and intakes of diuretics, thrombolytics and β -blockers

Table 4: Risk of Arrhythmias and Its Severity Associated with Hypokalemia

Quartiles of serum K (mmol/l)	Patients without arrhythmias (n=144)	Supra-ventricular (n=64)	OR (95%CI) <i>p value</i>	Ventricular arrhythmias (n=66)	OR (95%CI) <i>p value</i>
Q1 <3.5 (n=84)	23	20	2.4 (1.1 - 5.1)* <i>p=0.02</i>	41	8.3 (4.0 - 16.6)* <i>p=0.001</i>
Q2 3.5-4.2 (n=95)	50	24	1.1 (0.6 - 2.1)* <i>p=0.243</i>	21	0.96 (0.5 - 1.8)* <i>p=0.909</i>
Q3 4.3-5.1 (n=51)	33	14	0.63 (0.28 - 1.3)* <i>p=0.25</i>	4	0.20 (0.07- 0.58)* <i>p=0.87</i>
Q4 >5.1 (n=44)	38	5	0.43 (0.21 - 0.98) <i>p=0.76</i>	1	0.32 (0.09 - 0.67) <i>p=0.85</i>

*Adjusted for obesity, hypertension, gender, smoking and intakes of diuretics, thrombolytics and β -blockers

DISCUSSION

It has been well documented that the ischemic heart appears to be particularly vulnerable to hypokalemia and is therefore at greater risk for arrhythmias. In this study, serum potassium value <3.5 mmol/l was found in 84 (30%) of the AMI patients on admission. The incidence of hypokalemia, in this study, was higher than some previously reported studies (20%-27%)^{22,24}. The results of this study suggest that the incidence of arrhythmias was higher in AMI patients with hypokalemia compared to those with normokalemia (Table 1)¹⁸⁻²². Serum potassium on admission was decreased as the severity of arrhythmias was increased (Table 2). In addition, multiple logistic regression analysis showed that the risk of arrhythmias in the lowest quartile of serum potassium compared with the highest quartile of serum potassium was significantly increased by 4.7 fold.

The risks of supra-ventricular and ventricular arrhythmias were significantly increased by 2.4, and 8.3 folds respectively, in patients with serum potassium levels at the lowest quartile compared with the highest quartile of serum potassium (Table 4). These results indicate a clear concentration effect for potassium and raise the possibility that mild reductions of potassium can cause arrhythmias in AMI patients. The physiological mechanisms that may account for the relationship of hypokalemia to cardiac arrhythmias are not fully explained; however, it has been suggested that low extracellular potassium could increase automaticity (increased slope of diastolic depolarization) resulting in a decreased conduction velocity. In animal studies, it has been shown that hypokalemia precipitates reentrant cardiac arrhythmias by decreasing conduction, increasing refractoriness and unidirectional block²⁵. In addition, biochemical factors including catecholamines and size of infarction with neural influences may also play important arrhythmogenic roles²⁶⁻²⁹.

In this study, β -blocker treatment prior to admission seems to have beneficial effect. The number of patients taking β -blockers was significantly increased in those without arrhythmias than those with arrhythmias and the percentage of patients on β -blocker was significantly decreased as the severity of arrhythmias was increased (Table 2). In addition, patients on β -blockers had higher admission serum potassium levels than others without. Hypokalemia may arise as a result of the profound catecholamine drive that occurs at the onset of infarction and could be purely epiphenomenal to arrhythmias. Catecholamines are involved in the regulation of the distribution of potassium as β -2-agonists lower plasma potassium (by increasing cellular uptake of potassium) and alpha- agonists increase plasma potassium concentration. Activation of the sympathetic nervous system can provoke arrhythmias by increasing the automaticity of cardiac cells, increasing triggered activity in the heart and promoting the development of hypokalemia³⁰⁻³³. This may suggest that catecholamine-mediated fall in extracellular potassium is contributing to the observed hypokalemia in patients with arrhythmias.

In this study, the number of patients on diuretics was greater in those with arrhythmias than those without arrhythmias, but this was not statistically significant and the serum potassium was not statistically different between patients taking diuretics compared with those who are not. This is consistent with other studies suggesting that diuretics have no impact on the serum potassium levels on admission in AMI patients³⁴. However, other studies suggested an association with the use of thiazide diuretics with the risks of primary cardiac arrest³⁵⁻³⁷. It has been suggested that the most important and frequent metabolic side effects of diuretics is hypokalemia causing ventricular arrhythmias and development of hypokalemia. It was reported to be associated with use of diuretics in patients with coronary heart disease and could be associated with life-threatening arrhythmias, prompt recognition and correction of hypokalemia has been recommended for patients with cardiovascular diseases presented to the emergency department³⁸⁻³⁹.

In this study, the most important predictor of serum potassium was the heart rate on admission. Indeed tachycardia has been reported to predict the tendency to develop arrhythmias and it is suggested to be a non-invasive measurement of cardiac autonomic modulation⁴⁰.

The association between hypokalemia and severity of arrhythmias observed in this study emphasize a need for admission testing of serum potassium in patients with AMI. However, the treatment of patients with hypokalemia on admission must be fully monitored as high potassium levels on the other hand can contribute to the arrhythmias and avoiding both hypo- and hyperkalemia is beneficial in cardiovascular diseases⁴¹.

CONCLUSION

This study had established an association between hypokalemia and severity of arrhythmias occurring early after myocardial infarction. Furthermore, the results of this study reveal an apparent concentration effect for potassium and suggest that mild reductions of potassium can be directly causing arrhythmias and may contribute to the severity of arrhythmia in AMI patients. The association between hypokalemia and arrhythmias was independent of other patient characteristics. A large study is required to investigate the potential benefit of screening and controlling serum potassium levels of AMI patients on admission.

Submission date: 25.10.2010. Acceptance date: 27.1.2011

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