

Original Research Article

Study of impact and association of Serum Potassium Levels with the incidence of risk of Atrial Fibrillation

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Abstract

Background: Atrial fibrillation is the most common sustained arrhythmia in the elderly. Serum potassium is associated with ventricular arrhythmias and cardiac arrest. Hypokalemia causes cellular hyperpolarity, increases resting potential, hastens depolarization and increases automaticity and excitability. Thus, electrolyte imbalances and hypokalemia may contribute to the etiology of Atrial Fibrillation.

Aim and objectives: The objective of this study was to investigate the association of serum potassium levels and the risk of atrial fibrillation in a population based setting.

Material and methods: The study was performed within the prospective population-based setting. The study population consisted of 1000 participants without atrial fibrillation at baseline for whom baseline levels of serum potassium were measured. Atrial fibrillation was ascertained from centre visit, ECG assessments as well as medical records.

Results: During one year of study, total 1000 patients were analyzed, 64.6% of the hypokalemic patients developed atrial fibrillation. Participants with hypokalemia (64.6%) (< 3.5 mmol/l) had a higher risk of atrial fibrillation than those with normokalemia (24%) (3.5–5.0 mmol/l). This association was independent of age, sex, serum magnesium and other potential confounders.

Conclusion: In this study low serum levels of potassium were associated with a higher risk of atrial fibrillation.

Key words

Serum potassium levels, Atrial Fibrillation, Hypokalemia.

Introduction

Atrial fibrillation is the most common sustained arrhythmia in the elderly. Atrial fibrillation is associated with a 3 to 5 times higher risk of stroke [1] and with a higher risk of heart failure, cardiac mortality and total mortality [2, 3]. Serum potassium, especially hypokalemia (< 3.5 mmol/l) is suggested to be associated with a higher risk of cardiovascular disease, especially ventricular arrhythmias and cardiac arrest [4]. Few studies previously investigated the association of serum potassium with the risk of atrial fibrillation [5–8].

Potassium plays an important role in cardiac electrophysiology [9]. Serum potassium concentrations are commonly low following cardiac surgery [10] and appear marginally lower in non-surgical cohorts among those suffering atrial arrhythmias [11].

Clinical studies showed that lower serum potassium levels were associated with a higher perioperative risk of atrial fibrillation [5, 8]. One study in haemodialysis patients found low serum potassium to be associated with an increase in P-wave duration, a marker of atrial conduction [12]. P-wave duration increase has been associated with a higher risk of atrial fibrillation [13–17]. This supports the hypothesis that serum potassium is involved in atrial conduction and possibly atrial fibrillation. However, as results from clinical studies may not be generalizable to the general population, results from a population based cohort study with a large sample size are relevant.

Therefore, the objective of this study was to investigate the impact and association of serum potassium levels with the incidence of risk of atrial fibrillation in a population-based setting.

Materials and methods

Study duration: One year from December 2018 to December 2019.

Study population: The current study was a population-based prospective cohort study, designed to examine the onset of risk factors for disease in older adults. Total 1000 patients were assessed and all aged 45 years and over were included in the study. Serum Potassium and resting Electrocardiogram (ECG) were performed on every patient. The medical ethics committee approved the study and all participants gave informed consent.

Serum potassium levels: Blood samples were drawn by venepuncture from non-fasting patients and collected in 5 ml plain vials from which serum was separated by centrifugation. Serum potassium levels were measured by fully automatic NuLYTE Electrolyte Analyzer within our clinical chemistry department using standard methods and expressed as mmol/l.

Assessment of atrial fibrillation: We used ECGs that were obtained at baseline and during follow-up examinations. All ECGs were processed by the Modular ECG Analysis System (MEANS). Atrial fibrillation occurring during a serious disease resulting in death, during myocardial infarction or during cardiac operative procedures of patients who recovered during the hospital admission was not included as cases. We did not distinguish between atrial fibrillation and atrial flutter when we identified cases because both conditions are very similar with respect to risk factors and consequences.

Results

The population for analysis consisted of 1000 patients. The most common age group of the population was 66 to 75 years (42.3%) (**Table - 1**) and included 520 (52%) of females (**Table - 2**). 646 (64.6%) patients developed atrial

fibrillation (**Table - 3**). The mean serum potassium level ranged from 2.40 to 5.51 mmol/l.

Compared to patients with normokalemia (24%), those with hypokalemia (64.6%) were more likely to be female (50.7%) (**Table - 2**), to use low-ceiling diuretics or to use beta-blocking drugs and were less likely to smoke. Also

patients with hypokalemia had higher systolic and diastolic blood pressure, lower total cholesterol and had a longer P-wave duration after adjustment for age and sex.

Out of 1000 patients, hypokalemic patients were at higher risk of atrial fibrillation (64.6%) than those with normal values (24%) (**Table - 3**).

Table - 1: Age group distribution.

| Age group | Serum potassium levels | | | Grand total |
|-------------|------------------------|--------------|--------------|-------------|
| | Hypokalemia | Normokalemia | Hyperkalemia | |
| 45-55 years | 132 | 16 | 03 | 151 |
| 56-65 years | 169 | 33 | 13 | 215 |
| 66-75 years | 241 | 105 | 77 | 423 |
| > 75 years | 104 | 86 | 21 | 211 |
| Total | 646 | 240 | 114 | 1000 |

Table - 2: Gender distribution.

| Gender | Serum potassium levels | | | Grand total |
|--------|------------------------|--------------|--------------|-------------|
| | Hypokalemia | Normokalemia | Hyperkalemia | |
| Male | 318 | 134 | 28 | 480 |
| Female | 328 | 106 | 86 | 520 |
| Total | 646 | 240 | 114 | 1000 |

Table - 3: Association of Serum potassium levels with risk of Atrial fibrillation.

| Serum Potassium (mmol/l) | Number of patients having Atrial Fibrillation | % of patients having Atrial Fibrillation |
|--------------------------|---|--|
| Hypokalemia (< 3.5) | 646 | 64.6 % |
| Normokalemia (3.5-5.0) | 240 | 24 % |
| Hyperkalemia (> 5.0) | 114 | 11.4 % |
| Total | 1000 | 100 % |

Discussion

According to recognised international criteria, atrial fibrillation is defined as an episode of AF lasting ≥30 seconds that is clinically detected and/or electrocardiographically confirmed (on a 12-lead ECG) [18]. In this study, low levels of serum potassium levels were associated with a higher risk of atrial fibrillation. This association was independent of several potential confounders. We found that hypokalemia (64.6%) (<3.5mmol/l) was associated with an increased risk of atrial fibrillation in comparison to normokalemia (24%).

Several studies previously investigated the influence of potassium in the development of atrial fibrillation. Also in a study among 2402 patients undergoing cardiac surgery, preoperative hypokalemia (<3.5 mmol/l) was associated with atrial fibrillation compared to higher levels of atrial fibrillation [5]. A study of 253 patients undergoing cardiac surgery, showed an association between lower serum potassium (<3.9 mmol/l) and an increased risk of atrial fibrillation during the postoperative period [8]. In one study in 517 patients with an acute myocardial infarction, hypokalemia was not associated with a higher risk of atrial fibrillation

during hospitalization compared to normokalemia [6], but these differences in results may be caused by a lack of power or by differences in populations as patients with an acute myocardial infarction may not be comparable to the general population or to a population undergoing cardiac surgery. In addition we found that especially in patients with a history of myocardial infarction, low serum potassium was associated with a higher risk of atrial fibrillation. Although these subgroup analyses were based on small numbers, this is further supported by other studies that suggest that especially cardiovascular patients are prone to develop ventricular arrhythmias or sudden cardiac death in case of low serum potassium [4].

Finally, we found that the association of low serum potassium with the risk of atrial fibrillation might be modified by the use of high-ceiling diuretics. High-ceiling diuretics can cause hypokalemia, thereby they might amplify the risk of atrial fibrillation in patients that are at lower levels of serum potassium. However the mechanisms behind these observed interactions have not been completely elucidated. We also found that low serum potassium is associated with an increase in P-wave duration, a marker of atrial conduction time in our study population. This has also been shown in a study in haemodialysis patients [12]. P-wave duration increase is associated with a higher risk of atrial fibrillation [13–17]. Although in our study, prolonged P-wave duration was associated with a higher risk of atrial fibrillation, this cannot solely explain how low serum potassium leads to an increased risk of atrial fibrillation as both P-wave duration and low serum potassium levels were independently associated with the risk of atrial fibrillation when added simultaneously in one model. The most likely mechanism through which serum potassium leads to an increased risk of atrial fibrillation is by the influence of potassium on the cell membrane potential. It is proposed that a low serum potassium level causes cellular hyperpolarization, increases resting potential and hastens depolarization [19].

Conclusion

This study with extensive follow-up showed that low serum potassium levels are associated with higher risk of atrial fibrillation. These results were obtained in the general population and were independent of several potential confounders. The proportion of cases due to low serum potassium may be low but as serum potassium is easily and frequently obtained this finding is still relevant at a population level, also because atrial fibrillation is relatively common and may have serious consequences such as stroke.

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