PRE-OPERATIVE SERUM POTASSIUM LEVELS AND PERI-OPERATIVE OUTCOMES IN PATIENTS UNDERGOING CARDIAC SURGERY.

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ABSTRACT

Although potassium is critical for normal electro physiology, the associations between pre-operative serum potassium level and peri-operative adverse events such as arrhythmias in cardiac surgery have not been examined in detail.

The objective of this study was to determine the prevalence of abnormal pre-operative serum potassium levels and whether such levels were associated with adverse peri-operative events in 50 patients undergoing coronary artery bypass grafting. Intra-operative and post-operative arrhythmias, the need for cardio-pulmonary resuscitation, cardiac death and death due to any cause prior to discharge from the post-operative intensive care unit were studied. The incidence for adverse outcome was 0.5% for death, 0.5% for cardiac death and 2% for cardio pulmonary resuscitation in patients with hypokalemia (serum potassium level < 3.5 meq. L⁻¹). Hypokalemia was found to be a predictor of serious peri-operative (OR: 2.2; 95% CI: 1.2-4.1) and post-operative arrhythmias (OR: 1.7; 95%CI: 1.0-2.7).

Pre-operative potassium repletion is low cost and low risk treatment measure and the data from this study suggests that screening and repletion be considered in patients scheduled for cardiac surgery.

KEY WORDS

Serum potassium, Cardiac surgery

INTRODUCTION

Potassium plays a central role in the maintenance of cellular polarization and is critical for the transmission of electrical impulses through the myocardium. Alterations in the normal balance between intracellular and extracellular potassium concentrations can lead to serious arrhythmias (1). The adverse association between hypokalemia and arrhythmias in animal models appears to be more significant in the presence of acute myocardial ischaemia (1,2). In patients with acute myocardial ischaemia, low serum potassium levels obtained on hospital admission are associated with the development of ventricular tachycardia or fibrillation (3,4). One study done on patients with coronary artery disease who underwent non-cardiac surgery suggested that a pre-operative serum potassium level of less than 3.5 meq/ L was

independently associated with peri-operative mortality (5).

When combined, these findings suggest that a pre-operative diagnosis of hypokalemia should delay the surgery until reversed. However such a recommendation is controversial since in two other studies no increase in the incidence of intra-operative arrhythmias occurred in patients with low serum potassium levels (6,7). This study prospectively evaluated the clinical outcome of various serum potassium levels in 50 patients who underwent elective coronary artery bypass grafting (CABG). The goals were to determine the prevalence of abnormal serum potassium levels pre-operatively and the incidence of adverse peri-operative events in this population, and to determine if there is a level of serum potassium that is associated with an increased risk of adverse outcomes.

MATERIALS AND METHODS

This prospective study was conducted at the St.John's Medical College Hospital on 50 patients who underwent elective CABG after obtaining an ethical committee clearance and informed patient consent. Exclusion criteria included patients who were on treatment with diuretics and patients with renal insufficiency. All the patients had serum potassium

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estimated on the morning of surgery. All the patients were anesthetized using a standardized anesthetic technique that included a benzodiazepine pre-medication. The conduct of cardiopulmonary bypass (CPB) was standardized in all the cases.

Baseline serum potassium level was defined as the pre-operative serum potassium level obtained on the morning of surgery. Patient demographics and clinical characteristics were recorded to identify which, if any, might predispose to alterations in serum potassium levels. Outcomes were defined as intermediate and final. Intermediate outcome included peri-operative arrhythmias, which were defined as any occurrence of intra-operative or post-operative arrhythmias. Intra-operative arrhythmias were defined as the occurrence of an arrhythmia serious enough to warrant treatment in the pre and post CPB periods. Post-operative arrhythmia events were identified by type and further sub-divided into ventricular arrhythmias (VA) and atrial arrhythmias (AA). A subset of patients who had both VA and AA were identified. The subset of patients requiring intra-operative treatment or having both VA and AA in the post-operative period was arbitrarily defined as experiencing serious peri-operative arrhythmias. This study did not include the occurrence of first-degree heart block, left or right bundle branch block, sinus bradycardia or sinus tachycardia. Final outcomes consisted of death, cardiac death and the need for cardiopulmonary resuscitation (CPR). Death was defined as mortality prior to discharge from the intensive care unit (ICU) for any cause (sepsis, multiorgan dysfunction syndrome). Cardiac death was defined as those patients whose death was considered to have been due to peri-operative myocardial infarction (MI), cardiac failure or cardiac arrhythmia and those who needed open chest CPR. CPR was defined as those patients who required closed chest cardiac massage or emergent electrical cardioversion in the post-operative period.

Descriptive statistics were generated for demographics, pre-operative characteristics, peri-operative arrhythmias and adverse outcomes. A histogram showing the pre-operative serum potassium levels was generated (Figure 1). To define a discrete level of serum potassium associated with peri-operative arrhythmias an odds ratio (OR) and a 95% confidence interval (CI) for each of the peri-operative adverse outcomes at serum potassium level thresholds of 3.0-3.5meq/L (by 0.1meq/L increments). Likewise, OR and 95% CI's were computed at serum potassium level thresholds of 4.5-5.5 meq/ L (by 0.1meq/ L increments).

These OR's were then recalculated adjusting for several potential confounders of the association between pre-operative serum potassium level thresholds and peri-operative outcomes. The adjusted confounders were sex, age and past history of arrhythmias, congestive heart failure and hypertension. The hypokalemic analysis was initially completed on all patients with a pre-operative potassium level of less than 3.5meq/L and the hyperkalemic analysis on all patients with pre-operative serum potassium levels of 5.5 meq/ L or more. These initial analyses were confirmed using the entire patient set (n=50). No adjustments were made for multiple comparisons. All statistical analysis was performed using the SPSS and EPI computer programs.

RESULTS

All 50 patients enrolled in this study were eligible for inclusion in the analysis. Serum potassium was normally distributed (Figure 1) with 3 (6%) patients having potassium levels below the traditional clinical threshold of 3.5meq/L. Patient characteristics within specific ranges of potassium values are listed in Table-1. Female sex, past history of arrhythmias and hypertension were commonly found in patients with lower potassium levels. Patient characteristics not associated with decreased serum potassium levels were age, weight and height, past history of congestive cardiac failure and ejection fraction of the heart. Elevated potassium levels were associated with a history of congestive cardiac failure and older age.

Peri-operative arrhythmias occurred in 50% of the patients, 10% having intra-operative arrhythmias. 15% of patients had post-operative ventricular arrhythmias and 17% of patients had post-operative atrial arrhythmias. Serious peri-operative arrhythmias occurred in 5% of patients. Pre-operative serum potassium values of less than 3.5 meq/L were associated with a higher incidence of arrhythmias (100%) than pre-operative potassium levels of above 3.5meq/L. Accordingly hypokalemia was defined as serum potassium level of less than 3.5 meq/L. Hypokalemia was a predictor of serious peri-operative

Fig. 1: Distribution of pre-operative serum potassium levels

arrhythmias (OR: 2.2; 95% CI: 1.2-4.1), intra-operative arrhythmia (OR: 2.0; 95%CI: 1.0-3.6) and post-operative AA (OR: 1.7; 95%CI: 1.0-2.7). Adjusting for age, sex and history of arrhythmia did not alter this relationship.

Serum potassium levels of more than 5.3 meq/L appeared to be associated with the development of post-operative AA. Overall the incidence for adverse outcome was 0.5% for death, 0.5% for cardiac death and 1.5% for CPR. All adverse outcomes occurred in patients with a pre-operative serum potassium level of < 3.5 meq/L. Univariate analysis yielded a strong trend towards an increased risk of death, cardiac death and CPR in low serum potassium level thresholds (< 3.5 meq/L). It was also interesting to note a significant crude association between potassium level threshold of less than 3.3 meq/L and the need for CPR (OR: 3.3, 95%CI: 1.2-9.5). However after adjusting for confounders, the significance of this association was lost.

This study has tried to validate an association between hypokalemia and the risk of adverse outcomes in cardiac surgery. At pre-operative levels of serum potassium between 3.5 and 5.5 meq/L there was no association between potassium level and the incidence of any type of peri-operative arrhythmia. However below this threshold the association became progressively stronger and occurred at levels of hypokalemia often considered safe by clinicians (3.3-3.5 meq/L). In addition pre-operative potassium levels of below 3.3 meq/L and above 5.3 meq/L showed a univariate association with the need for CPR. Although no conclusions regarding a causal relationship between pre-operative serum potassium level and adverse outcomes can be drawn from or with the presence of an abnormal serum potassium level before surgery can identify those patients at particular risk.

DISCUSSION

Significant elevations of extracellular potassium generally thought to be above 7.0 meq/L reduces the resting potential across the cell membrane and lead to an inability to conduct an electrical charge. Milder elevations of potassium levels have infrequently been found to be associated with development of arrhythmias. In laboratory investigations, Logic (8) found that regional hyperkalemia produced by intra-coronary infusion of potassium enhanced the likelihood of development of ventricular tachycardia and fibrillation. There is also a rare association between hyperkalemic periodic paralysis, a genetically inherited condition and the development of cardiac arrhythmias (9). Cooper *et al* (10) reported that hyperkalemia as well as hypokalemia was significantly associated with the development of ventricular fibrillation and tachycardia in patients admitted to a coronary care unit with the diagnosis of MI. The data in this study are inconclusive due to small sample size and confounding patient characteristics, but the potential association between hyperkalemia and the outcome of death, cardiac death and CPR deserves further investigation.

Decreases in extracellular potassium increase the duration of the action potential (increased phase 3 depolarization duration), increase automaticity (increased slope of diastolic depolarization) and decrease conduction velocity (10). These mechanisms may partly account for the relationship of hypokalemia to cardiac arrhythmias. Hypokalemia in laboratory models precipitates re-entrant cardiac arrhythmias by decreasing conduction, increasing refractoriness and unidirectional block (1). Dogs with hypokalemia have an abrupt lowering of the ventricular fibrillation threshold and experience frequent runs of ventricular tachycardia (11). More severe reductions in potassium levels result in spontaneous ventricular fibrillation in isolated

Table 1

Association between pre-operative serum potassium levels and patient characteristics

Pre-operative characteristics	Potassium level groups (meq/L)				
	3.0-3.4 (n = 3)	3.5-3.9 (n = 4)	4.0-4.4 (n = 27)	4.5-4.9 (n = 12)	5.0-5.5 (n = 4)
Age (Mean $\pm$ S.D.)	57.3 $\pm$ 9.7	60.8 $\pm$ 6.4	58.6 $\pm$ 8.6	59.2 $\pm$ 6.9	64.4 $\pm$ 6.3
H/o arrhythmias (%)	66	50	11	16	25
H/o hypertension (%)	100	50	60	50	50
Male: Female	1: 2	1: 1	1: 1	5: 1	1: 1

perfused rabbit hearts (1). However, the latter effect can be reversed by infusion of potassium suggesting that the reversal of hypokalemia may help to avert an adverse outcome (1). The ischaemic heart appears to be particularly vulnerable to hypokalemia and is therefore at greater risk for malignant arrhythmias. One of the most convincing data was provided by Hulting (12) who studied patients admitted to a coronary care unit with a diagnosis of MI and found that the incidence of ventricular fibrillation was 3.5% increasing to 8% in patients with hypokalemia ($<3.5\text{ meq/L}$). No episodes of ventricular fibrillation occurred when the serum potassium level was greater than 4.6 meq/L , but levels less than 3.9 meq/L were associated with a five-fold increase in the risk of ventricular tachycardia. Solomon *et al* (13) found an increase in the incidence of ventricular fibrillation in patients with potassium levels greater than 4.6 versus those with less than 3.0 meq/L which are quite contradictory to the findings of this study. Friedensohn *et al* (14) found a significant difference in serum potassium levels between those patients who did or did not develop malignant arrhythmias, but the difference could not be detected clinically (4.10 versus 4.19 meq/L with versus without arrhythmias).

These studies demonstrating the association between hypokalemia and serious arrhythmias indicate that pre-operative testing of serum potassium in patients with known ischaemic heart disease can identify patients who are at an increased risk for an adverse outcome. Delay of surgery until repletion of normal potassium levels would appear prudent were it not for two previous contradictory studies by Vietz *et al* (6) and Hirsh *et al* (7) of surgical patients that showed no association between hypokalemia and intra-operative arrhythmias. The findings in this study differ sharply from the findings of the afore mentioned studies. Reasons for these differences are that in this study the patient population had pre-existing cardiac disease and underwent cardiac surgery but the patients studied by Vietz *et al* (6) were relatively healthy and underwent non-cardiac surgery. Secondly the definition of arrhythmias in this study were those serious enough to warrant intervention while Vietz *et al* (6) and Hirsh *et al* (7) included any electronically detected arrhythmias. The higher incidence of hypokalemia reported by Vietz *et al* (6) and Hirsh *et al* (7) may reflect an acute redistribution of body potassium due to adrenergic influence of pre-operative anxiety rather than total body depletion. In our institute all patients undergoing cardiac surgery routinely receive sedative pre-medication and this negates the adrenergic influence of anxiety. Acute potassium redistribution increases the threshold for impulse generation as opposed to chronic potassium depletion that lowers the threshold (15,16).

The findings in this study showed that mortality occurred at a serum potassium level $< 3.5\text{ meq/L}$,

although not reaching statistical significance, agrees with the observation by Shah *et al* (5) that hypokalemia is independently associated with cardiac mortality. Hypokalemia therefore is independently associated with the risk of peri-operative arrhythmias and may predict the need for CPR. It is also reversible in contrast to virtually all other known risk factors for poor outcome such as age, sex, poor ejection fraction of the heart, diabetes mellitus and emergency surgery. Although the effect of potassium repletion on outcome was not studied, such treatment is relatively simple and inexpensive. A therapy as simple and inexpensive as potassium repletion may mitigate an adverse outcome in a large number of patients. The focus of this study was to examine the association between pre-operative serum potassium level and outcome. However this study has a few limitations. It did not attempt to control or track the electrolyte therapy that patients may have received peri-operatively. In addition magnesium levels were not determined in these patients and the study did not examine the fluctuations of potassium levels or its interactions with other electrolytes.

In summary, there was a significant association found between pre-operative serum potassium levels of less than 3.5 meq/L and peri-operative arrhythmias in patients undergoing elective CABG. Of the previously identified risk factors for adverse outcomes during cardiac surgery, such as age, sex and emergency procedures, hypokalemia may represent the only potentially reversible risk factor. Pre-operative potassium screening and repletion should be considered for patients scheduled for elective cardiac surgery. Both screening and therapy represent low risk and low cost prophylaxis.

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REFERENCES

1. Grumbach, L., Howard, J.W. and Merrill, L.L. (1954) Factors related to the irritation of ventricular fibrillation in the isolated heart: effect of calcium and potassium. *Circ. Res.* 2, 452-459.
2. Yano, K., Matsumoto, Y. and Hirata, M. (1991) Influence of sympathetic nerve activity on ventricular arrhythmogenicity in the dog with chronic hypokalemia. *Angiology*, 42, 878-888.
3. Nordrehaug, J.E. and von der Lippe, G. (1983) Hypokalemia and ventricular fibrillation in acute myocardial infarction. *Br. Heart J.*, 50, 525-529.

4. Johansson, B.V.V. and Dziamski, R. (1984) Malignant arrhythmias in acute myocardial infarction: relationship to serum potassium and effect of selective and non-selective beta blockade. *Drugs*, 28, 77-85.
5. Shah, K.B., Klienman, B.S., Rao, T.L., Jacobs, H.K., Mestan, K. and Schaafsma, K. (1990) Angina and other risk factors in patients with cardiac diseases undergoing non-cardiac operations. *Anesth. Analg.*, 70, 240-247.
6. Vitez, T.S., Soper, L.E., Wong, K.C. and Soper, P. (1985) Chronic hypokalemia and intra-operative dysrhythmias. *Anesthesiology*, 63, 130-133.
7. Hirsh, I.A., Tomlinson, D.L., Slogoff, S. and Keats, A.S. (1988) The overstated risk of pre-operative hypokalemia. *Anesth. Analg.*, 67, 131-136.
8. Logic, J.R. (1973) Enhancement of the vulnerability of the ventricle to fibrillation (VF) by regional hyperkalemia. *Cardiovasc. Res.*, 74, 501-507.
9. Gould, R.J., Steeg, C.N., Eastwood, A.B., Penn, A.S., Rowland, L.P. and De Vivo, D.C. (1985) Potentially fatal cardiac dysrhythmia and hyperkalemic periodic paralysis. *Neurology*, 35, 1208-1212.
10. Cooper, W.D., Kuan, P., Reuben, S.R. and Vanden Burg, M.J. (1984) Cardiac arrhythmias following acute myocardial infarction: associations with the serum potassium level and prior diuretic therapy. *Eur. Heart J.*, 5, 464-469.
11. Obeid, A.I., Verrier, R.L. and Lown, B. (1978) Influence of glucose, insulin and potassium on vulnerability to ventricular fibrillation in the canine heart. *Circ. Res.*, 43, 601-608.
12. Hulting, J. (1981) In hospital ventricular fibrillation and its relation to serum potassium. *Acta Med. Scand. Suppl.*, 647, 109-116.
13. Solomon, R.J. and Cole, A.G. (1981) Importance of potassium in patients with acute myocardial infarction. *Acta Med. Scand. Suppl.*, 647, 87-93.
14. Friedensohn, A., Faibel, H.E., Bairey, O., Goldbourt, U. and Schlesinger, Z. (1991) Malignant arrhythmias in relation to values of serum potassium in patients with acute myocardial infarction. *Int. J. Cardiol.*, 32, 331-338.
15. Wahr, J., Parks, R., Boisvert, D., Comunale, M., Fabian, J., Ramsay, J. and Mangano, D.T. (1999) Serum potassium levels and perioperative outcomes. *JAMA*, 281, 2203-2210.
16. Wong, K.C., Schafer, P.G. and Schultz, J.R. (1993) Hypokalemia and anesthetic implications. *Anesth. Analg.*, 77, 1238-1260.