The Korean Journal of Intermal Medicine
Vol. 5, No. 2, July, 1990

Determinants of Magnitude of Pseudohyperkalemia in Thrombocytosis

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The release of potassium from platelets is a well-known cause of pseudohyperkalemia in thrombocytosis. In predicting the magnitude of pseudohyperkalemia associated with thrombocytosis, previous investigations considered only the amount of potassium released from platelets during blood clotting, although the increment in serum potassium during blood clotting depends on the quantity of potassium released from platelets as well as the volume of distribution of the released potassium, which is inversely proportionate to the hematocrit. The present study proposes a new mathematical formula to predict the magnitude of increase in serum potassium during blood clotting, and accuracy of this formula has been tested in a patient with thrombocytosis.

Key Words: *Pseudohyperkalemia, Thrombocytosis*

INTRODUCTION

Platelets have high concentrations of potassium, and since part of it is released during blood clotting, serum potassium is therefore slightly higher than plasma potassium. In patients with thrombocytosis the amount of potassium released could be substantial, and serum potassium can increase significantly in vitro (pseudohyperkalemia). Pseudohyperkalemia has been reported in various thrombocythemic states including polycythemia vera, myeloproliferative disorders, acute and chronic myelocytic leukemia, and postsplenectomy thrombocytosis[1~11]. The degree of pseudohyperkalemia (the difference between serum and plasma potassium concentrations) clearly tends to be proportionate to the platelet count, but the other factors that influence the magnitude of pseudohyperkalemia are poorly understood. The present study considers the various factors that contribute to pseudohyperkalemia, proposes a new mathematical formula to predict its magnitude in thrombocytosis, and evaluates the accuracy of this formula in a patient with thrombocytosis due to polycythemia vera.

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MATERIALS AND METHODS

From each patient with thrombocytosis due to polycythemia vera and from 7 normal volunteers, 15 ml of blood was obtained with a standard plastic syringe. Within 10 seconds of the blood drawing, equal quantities were placed into 3 tubes: one containing potassium EDTA was used for measurement of hematocrit, platelet volumes and counts; one containing heparin was used for measurement of plasma potassium; and one containing no anticoagulant was used for measurement of serum potassium.

The heparin volume was negligible and had no discernible effect on potassium concentration. The

heparinized and coagulated blood samples were kept in the tube for one hour and then centrifuged at 3,000 rpm for 7 minutes to obtain serum and plasma for measurement of potassium. The potassium concentration was measured with a flame photometer, and platelet counts, mean platelet volume (MPV), and the hematocrit were measured with a Coulter counter.

RESULTS

The increase in potassium concentration due to clotting depends on the potassium concentration in the platelets and the percentage of that potassium released from the platelets during clotting. Potassium concentrations of platelets can be measured by two different methods. One utilizes platelet counts and potassium concentrations measured in platelet-rich and platelet-poor plasma, and the other utilizes measurement of potassium concentrations and platelet counts in plasma-free platelet buttons. The latter method was used in the present study because the former method involves two measurements and therefore is more prone to error. The potassium concentration is 0.84 mEq/10^{12} platelets according to Ingram et al.[4] and 0.8 mEq/10^{12} platelets according to Nilsson et al[3].

We used the mean of these two values, 0.82 mEp/10^{12} platelets.

The fraction of potassium released from the platelets during blood clotting is calculated as the difference between serum and plasma potassium divided by the total platelet potassium content. The latter was estimated from platelet counts in 7 normal subjects. The average platelet count was 263,000/mm^3, and the average difference between their serum and plasma potassium was 0.197 mEq/L. The estimated potassium content of the platelet is $0.82 \times 0.263 = 0.215$ mEq/L (Table 1). If this estimated amount were added to the serum in a liter of blood (0.56 liter, given a hematocrit of 44%), the serum potassium concentration should increase by $0.215/0.56 = 0.384$ mEq/L. Since the actual increase was 0.197 mEq/L, the estimated % of potassium is $0.197/0.384 = 51.3\%$.

A formula can be derived to predict the magnitude of pseudohyperkalemia if the following are known: (1) the total potassium content estimated from platelet counts, (2) the fraction of potassium released during clotting and (3) the volume of distribution of the released potassium calculated from the hematocrit.

Thus,

(serum-plasma) potassium = (platelet potassium content × % released)/serum volume

1. The platelet potassium content in 1 liter of blood = 0.82 mEq × number of platelets in millions/mm^3*.

2. The fraction of platelet potassium released during clotting is assumed to be 0.513 (capable of increase with time).

3. The serum volume in liters = (100 − hematocrit)/100.

Hence,

$$\text{Magnitude of pseudohyperkalemia (mEq/L)} = \frac{(\text{platelet count in MM/mm}^3 \times 0.82 \times 0.513)}{(100 - \text{hematocrit})/100}$$

*Sine 0.82 mEq of potassium are contained in 10^{12} platelets, the amount of potassium in the platelet in 1 liter of blood can be calculated as follows:

0.82 mEq × platelet number in 1 liter/10^{12} = 0.82 mEq × platelet number/$mm^3 \times 10^6/10^{12}$ = 0.82 mEq × platelet number in millions × $10^6/mm^3 \times 10^6/10^{12}$ = 0.82 mEq × platelet number in millions/$mm^3 \times 10^{12}/10^{12}$ = 0.82 mEq × platelet number in millions/mm^3.

In Table 2, the predicted increases in serum

Table 1. Calculation of % Potassium Released During Blood Clotting in Normal Controls (n=7)

Serum minus plasma potassium :	0.197 mEq/L
Platelet count :	263,000/mm^3
Hematocrit :	44%
% potassium released during blood clotting : 51.3%	

Table 2. The Difference Between Serum and Plasma Potassium Concentration

Data	Serum K* (mEq/L)	Plasma K* (mEq/L)	Platelet $10^6/mm^3$	Hct** (%)	Difference in K* (mEq/L)	Expected Difference (mEq/L)
9/26	6.4	4.5	1,412	67	1.9	1.80
10/7	5.5	4.5	1,116	49	1.0	0.92

K* : potassium Hct** : hematocrit

potassium using the above formula are compared with those obtained from the actual measurements in a patient with polycythemia vera. It is clear that the above formula predicts a more reliable estimate of pseudohyperkalemia than the platelet count alone.

DISCUSSION

In predicting the magnitude of pseudohyperkalemia associated with thrombocytosis, previous investigations considered only the amount of potassium released from the platelets during blood clotting. The amount of potassium released during clotting depends on two factors: the amount of potassium in the platelets and the fraction released. The potassium content of the platelets depends mainly on the number of platelets, but size can play a role. For example, in a patient with megakaryocytic leukemia reported by Hartmann et al., pseudohyperkalemia (serm potassium 10 mEq/L) was associated with a platelet count of only 642, 000/mm^3[2]. In most instances, however, the size of the platelet does not seem to vary much.

In our study of 8 hospitalized patients and 7 normal controls, the variation in MPV (mean platelet volume) was less than 20%. To a much smaller extent, the amount of potassium for a given weight of platelets may depend on the cause of thrombocytosis. In normal subjects, potassium per kg of wet weight of platelets was 69.1 mEq, whereas the figures were 71.2 mEq, 74.8 mEq, and 76.1 mEq, respectively, for chronic myeloid leukemia, myeloid metaplasia, and polycythemia vera[2].

The percentage of potassium released from each platelet during clotting and the rapidity of its release may also depend on the cause of thrombocytosis; it has been suggested that potassium release occurs more readily in patients with polycythemia vera and myeloproliferative disorders than in normal patients and in other hematological disorders[2,3]. Whether the observed difference in the degree of pseudohyperkalemia with different types of thrombocytosis is due to differences in the speed of degranulation or absolute differences in the fractional potassium release is not known. In the former case, the extent of pseudohyperkalemia would depend on the duration of the delay before the serum is separated.

It is quite apparent that the increment in serum potassium during blood clotting would not only depend on the quantity of the potassium released from the platelets but also on the volume of distribution of the released potassium, i.e., fraction of serum volume, which is inversely proportionate to the hematocrit. Since the hematocrit can vary from <70% to> 70%, % serum volume could vary from <30% to> 90%. Consequently, for a given amount of potassium released, an increment in serum potassium during clotting will be three times as great in a person with a hematocrit of 70% (serum volume 30%) as in a person with a hematocrit of 10% (serum volume 90%). This could explain why pseudohyperkalemia tends to be more severe in polycythemia vera, which is characterized by high hematocrits, than in conditions associated with low hematocrit, such as chronic myelocytic leukemia[2,4].

In the patient with polycythemia vera (Table 2), the degree of pseudohyperkalemia was much greater (two-fold) when the hematocrit was 67% than when it was 49%, and the platelet count was also lower with the lower hematocrit, but the difference in platelet count can explain only about 30% of the discrepancy in pseudohyperkalemia. Clearly, the magnitude of pseudohyperkalemia is much better predicted when both hematocrit and platelet count are taken into consideration.

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