ORIGINAL ARTICLE

Transport and temperature effects on measurement of serum and plasma potassium

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SUMMARY

Transport of blood samples from general practice to a central laboratory can result in spuriously high or low potassium concentrations. The importance of this phenomenon was studied in a general practice serving a population of 15 000 patients, 27 km from the pathology laboratory that routinely measured serum potassium. The design involved comparison of potassium levels between control serum (plain gel-separation serum tubes centrifuged in the surgery), routine serum (plain gel-separation tubes centrifuged in the laboratory) and routine plasma samples (lithium–heparin tubes centrifuged in the laboratory).

Complete triple sets of data were obtained for 371 samples. Altman and Bland plots for the control serum *vs* routine serum samples showed a mean difference of +0.1 mmol/L with limits of agreement (± 2SD) +0.6 mmol/L, −0.4 mmol/L and for control serum *vs* routine plasma a mean difference of +0.2 mmol/L with limits of agreement +0.8 mmol/L, −0.4 mmol/L. There was a negative association between mean weekly routine plasma potassium levels with mean weekly temperatures achieved. Regression analysis indicated that both maximum temperature achieved and time to centrifugation significantly contributed to differences observed in the routine plasma samples, but not with the routine serum samples. For plasma samples exposed to high temperatures a clinically significant lowering of potassium concentrations can arise.

These results confirm that spurious lowering of potassium concentrations occurs in plasma samples collected in a primary care setting. The preferred method is to centrifuge samples soon after venepuncture. Where this is not possible, collection into plain gel-separation tubes (serum) ensures less variation due to temperature and time to centrifugation than does collection into lithium–heparin tubes (plasma).

INTRODUCTION

The phenomenon of spurious hyperkalaemia recorded in blood samples that have undergone haemolysis before analysis is well recognized[1–3]. However, recent reports highlighted the possibility that high ambient temperatures can cause spurious hypokalaemia[4,5]. In these studies mean daily plasma potassium levels from UK hospital patients were compared with those of patients from general practice from January to August. The mean plasma potassium levels derived from general practice fell in relation to hospital mean plasma potassium levels as the ambient temperature increased; thus transportation of samples from general practice seemed to account for a substantial degree of hypokalaemia.

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It would appear that errors in the measurement of potassium levels are possible in both directions and that transportation effects and ambient temperature play a crucial part in the stability of blood potassium levels. A study was designed to determine the effects of transportation during the day-to-day service commitment of a general practice situated some distance from the analysing laboratory.

METHOD

The setting was the Honiton Group Practice, serving a semirural population of 15 000 patients and situated 27 km from the central pathology laboratory in Exeter. The Exeter service routinely measures serum potassium. Blood samples were drawn into paired plain clotted blood tubes with gel-separation plugs and into a lithium–heparin tube by means of the Sarsted venepuncture system. One plain tube (control serum sample) was allowed to clot at room temperature and centrifuged within 30 min of venepuncture, in the surgery, with a non-swing-arm centrifuge (Sarsted). The other plain tube (routine serum sample) and the lithium–heparin tube (routine plasma sample) were labelled and packaged in the normal manner. All three were transported in plastic specimen boxes by the hospital courier service; collection time was 1300 h each weekday. Time from venepuncture to centrifugation for the routine serum and routine plasma samples in the central laboratory was recorded. A robust electronic maximum–minimum thermometer was included in each courier collection box and the maximum temperature reached by the samples was recorded on arrival at the laboratory.

The data were analysed by the method of Altman and Bland[6] for comparing different methods of measurement. Regression analysis, examining the effects of maximum temperature achieved and time to serum or plasma separation, was performed with the SPSS for Windows statistical package.

The project had approval from the local research ethics committee.

RESULTS

Complete data sets were obtained for 371 triple control serum/routine serum/routine plasma samples. Time from venepuncture to centrifugation of routine serum and routine plasma samples ranged from 2 h 47 min to 12 h 18 min, mean 5 h 52 min. Maximum temperatures achieved ranged from 15 to 30 °C with temperatures following a Gaussian distribution.

Mean concentrations of potassium in the control serum, routine serum and routine plasma samples were 4.2, 4.1 and 4.0 mmol/L, respectively. Analysis of variance indicated a significant difference between these groups (F=38.88, $P<0.001$). *Post-hoc* tests indicated that while there was no significant difference between the control serum and routine serum samples ($P>0.05$), routine plasma samples were significantly lower than control serum ($P<0.001$). Only 4.3% of routine serum results fell outside the normal laboratory range of 3.5–5.5 mmol/L, with no results in the hyperkalaemic range.

Control serum and routine serum potassium values showed significant correlation (r=0.842, $P<0.001$) as did routine plasma and control serum potassium values (r=0.725, $P<0.001$). Altman and Bland plots for both comparisons are shown in Figure 1(*a*) and (*b*).

The control serum/routine serum plot produced a mean difference between the two methods of 0.1 mmol/L with limits of agreement (±2SD) being +0.6 mmol/L and −0.4 mmol/L. The control serum/routine plasma plot produced a mean difference between the two methods of +0.2 mmol/L with limits of agreement (±2SD) being +0.8 mmol/L and −0.4 mmol/L.

Regression analysis indicated that neither maximum temperature recorded nor time to serum separation was a significant predictor variable in the routine serum method. However, for routine plasma samples maximum temperature recorded exerted a significant effect and time to plasma separation also contributed to the difference observed ($P<0.0001$), expressed in the following formula: difference observed − 0.29+(0.03 × max temp) − (0.00001 × time) (temperature in degrees Celsius and time in hours).

Consequently, increasing maximum temperature achieved and, to a small degree, time to plasma separation contributed to depression of potassium values in the routine plasma samples. The effect of mean weekly maximum temperatures achieved during transportation on the mean weekly routine plasma potassium levels is shown in Figure 2.

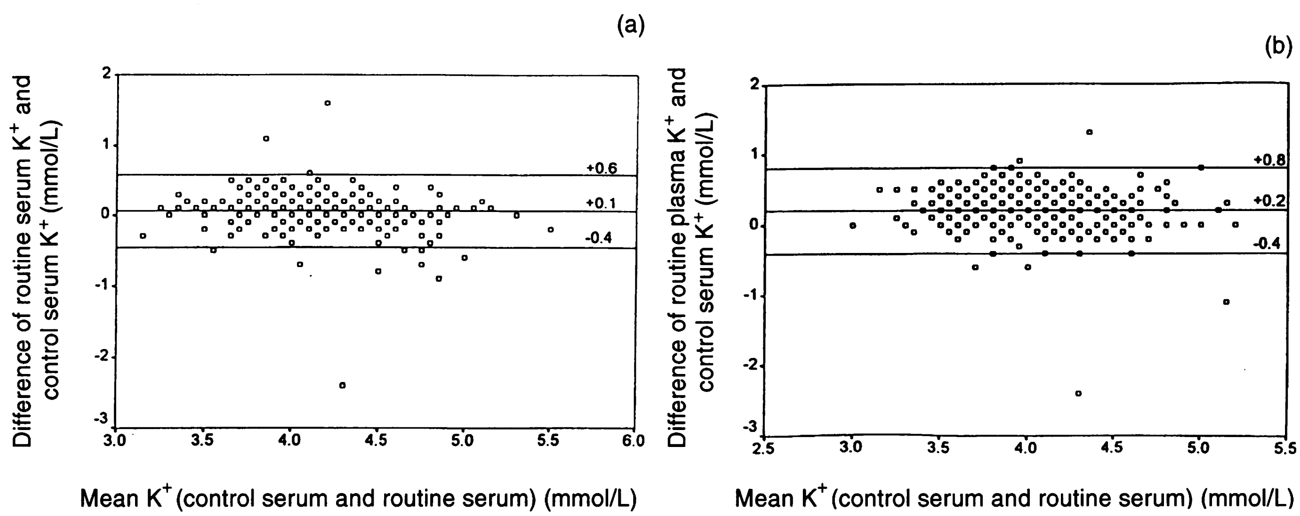

Figure 1 **Difference against mean for control serum and routine serum potassium values (*a*) and for control serum and routine plasma values (*b*).** Lines show mean and ±2SD

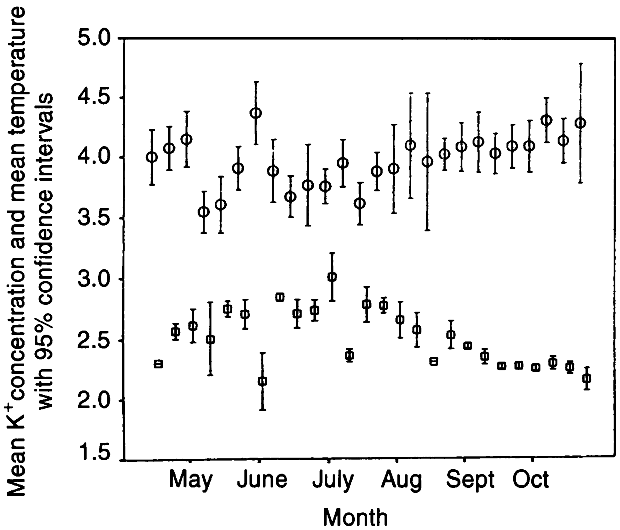

Figure 2 **Effect of mean weekly temperatures achieved during transportation on mean weekly routine plasma potassium concentrations.** ○=routine plasma K^+(mmol/L); □=maximum temperature °C/10.

DISCUSSION

This study confirms the previous observations that a temperature effect results in spuriously lowered plasma potassium concentrations in samples not immediately centrifuged[4,5].

The Altman–Bland method of analysis was employed for the reasons discussed by Hollis[7]. The Altman–Bland analyses indicate closer mean values and tighter limits of agreement for the routine serum samples than for the routine plasma samples. The lower mean value of the plasma samples may be partly explained by the slightly lower reported normal ranges for plasma potassium than for serum potassium, but the wider limits of agreement are explained by temperature effects and time elapsed to plasma separation as discussed below.

The regression analyses indicate that both time to plasma separation and maximum temperature achieved by the sample contribute significantly to the depression of potassium levels observed in the routine plasma samples. These effects did not contribute significantly to variations observed in the routine serum samples.

The graph illustrating weekly mean plasma potassium levels plotted against weekly maximum temperatures achieved by the samples (Figure 2) shows a variable trace inversely related to weekly mean sample temperature.

What is the clinical significance of the observed effects? With only 4.3% of control serum potassium values falling outside the normal laboratory range, a meaningful sensitivity/specificity analysis was not possible. However, this study illustrates that spuriously low potassium concentrations do occur in plasma samples collected in primary care, and this phenomenon may cause clinical uncertainty. Conventionally, test reference ranges are set as the mean value $\pm$2SD. Consequently 2.5% of normals are cut off at each end of the range, and 2.5% of un-diseased people in a population will have a low potassium result. In this study the order of magnitude of the observed temperature effect is about one standard deviation of the normal range. With approximations, the proportion of un-diseased people in the population with a low potassium could rise from 2.5% to 15% in very hot weather. Likewise, although no cases of hyperkalaemia were detected in this study it is likely that the spurious lowering of potassium levels in plasma samples would lead to an underestimation of the proportion of raised potassium levels in a population.

The small variation in potassium values reflects the general practice population, and greater variations would be expected in a hospital population with more critically ill patients. In this setting the conclusions regarding use of dry-gel separation tubes and minimizing time to serum separation are even more relevant.

In conclusion, the preferred method of transporting samples for potassium determination is to centrifuge samples soon after venepuncture. If this is not possible then collection into plain gel-separation tubes (serum) would ensure less variation due to temperature change and time to centrifugation than collection into lithium–heparin tubes (plasma).

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