Clin Chem Lab Med 2009;47(7):880–881 © 2009 by Walter de Gruyter • Berlin • New York. DOI 10.1515/CCLM.2009.190

Letter to the Editor

Hyperleukocytosis: pseudohyperkalaemia and other biochemical abnormalities in hyperleukocytosis

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Keywords: hyperleukocytosis; pseudohyperkalaemia.

A 66-year-old woman, recently diagnosed with T cell prolymphocytic leukaemia (PLL) was admitted for cytotoxic therapy, with a potassium (K^+) of 5.5 mmol/L on admission as measured on a lithium heparin plasma sample (Beckman DxC800; Beckman Coulter Diagnostics, Fullerton, CA, USA). The sample was analysed within 70 min of collection. The white blood cell count (WBC) was 460×10^9/L (Sysmex XE-5000; Sysmex, Kobe, Japan). The full biochemistry results excluded acidosis, renal failure, tumour lysis syndrome, IV contamination, haemolysis, or EDTA contamination, and the patient had a normal ECG. The elevated K^+ result led to commencement of resonium to lower the K^+, and this continued until day 2. Resonium (A) is a cation-exchange resin which lowers the blood potassium level by exchanging potassium for sodium in the intestine. On day 2, a K^+ of 9.0 mmol/L was obtained, and the result was immediately phoned to the clinical unit. The medical staff were appropriately notified that this result was probably artefactual and the resonium was ceased after a venous blood gas sample was collected, and a K^+ of 4.0 mmol/L obtained (Rapidlab 1265; Siemens Healthcare Diagnostics, Medfield, MA, USA).

Pseudohyperkalaemia is well-documented in hyperleukocytosis, particularly with chronic lymphocytic leukaemia (CLL) (1–3). Despite most haematologists and emergency physicians being aware of this phenomenon, under some circumstances hyperkalaemia might be misinterpreted. We frequently observe initiation of treatment to lower K^+, usually in Emergency or Haematology Units, with the potential to cause in vivo hypokalaemia. Unfortunately, they are not aided in a timely manner in many instances by biochemistry staff who do not routinely check for elevated white blood cell (WBC) with elevated K^+.

In CLL, leukocytes exhibit increased fragility to mechanical stresses (4). This phenomenon has also been observed with acute lymphoblastic leukaemia (ALL) (5–7), and PLL (8). Even minor mechanical stress, such as prolonged tourniquet application, vacutainer collection, vigorous aspiration or dispensation through a syringe, centrifugation or shaking by hand, or transport via pneumatic systems (accelerating or decelerating rapidly) can result in cell lysis and release of cellular contents [K^+, lactate dehydrogenase (LDH), aspartate transaminase (AST)], as demonstrated by our data (Table 1). Additionally, delays in centrifugation, especially of unrefridgerated specimens, prior to analysis will result in significant changes to the K^+, LDH and glucose concentrations. The glucose on the blood gas analyser indicated the presence of interfering substances. The patient had received paracetamol which is documented as an interfering substance in the analyser manual.

It is well known that K^+ is higher in serum due to platelet release as a result of platelet rupture during the clotting process (9). For this reason, plasma is the preferred sample for the determination of K^+ concentration (9). As demonstrated by our data, in samples with markedly elevated WBCs, serum provides more accurate estimate of K^+, LDH and AST. A likely reason is the clotting process locks the WBCs in the clot, eliminates cell movement during mechanical stress processes and minimises lysis. Although others have postulated the converse: that the clotting process increases rupture of fragile leukocytes and results in increased release of K^+ (10).

In summary, in patients with hyperleukocytosis, serum and venous blood gas samples may provide more accurate estimates of K^+ and other analytes, compared to lithium heparin plasma. Tubes containing gel separator may be preferred to minimise cellular contact with plasma post centrifugation. Samples must be analysed with minimal delay, and pneumatic transport systems should not be used to transport samples. High K^+ results should be urgently rechecked, taking into account the above specimen requirements before potentially misguided K^+ lowering therapy is instituted. Finally, as these data were obtained from a single patient, the results may not be valid for all patients. Laboratories should consider completing studies on their own patients using their

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Table 1 Results of samples collected on different days, plus samples transported by different modes and collection devices.

Analyte	On admission	Day 2	Day 2 – venous blood gas (2.5 h later)	Day 8 – sample comparison						Reference interval
				Venous blood collected in Greiner bio-one vacutainer tubes. Samples A, B and C analysed within 45 min of collection					Venous blood gas collected in Rapidlyte syringe (Siemens)	
				Plasma A	Plasma B	Plasma C	Plasma D	Serum	Analyzed within 15 min	
Na^+	138	138	139	140	134	141	139	141	140	135–145 mmol/L
K^+	5.5	9.0	4.0	4.1	11.4	4.3	6.4	3.6	3.5	3.5–4.5 mmol/L
Cl^-	106	108	105	107	107	108	109	108	107	100–110 mmol/L
Glucose	5.0	5.0	4.7[a]	5.2	5.0	5.2	5.0	5.4	4.7[a]	3.0–7.8 mmol/L
AST	22	42		71	79	67	74	65		<31 U/L
LDH	818	947		1041	1476	1022	1241	926		150–280 U/L
RBC	2.72	2.64		2.48						$3.8–5.2\times10^{12}$/L
WBC	456	403		440						$4–11\times10^{9}$/L
Platelet	28	27		15						$140–400\times10^{9}$/L

A, non-gel tube hand delivered; B, non-gel tube sent via pneumatic system; C, gel tube hand delivered; D, non-gel tube, hand delivered allowed to stand for 45 min; [a]interfering substances.

own collection tubes under their own particular pre-analytical conditions to determine the effects.

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