Pediatr Nephrol (2006) 21:301–302
DOI 10.1007/s00467-005-2088-1

LETTER TO THE EDITORS

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Spurious hyperphosphatemia in a patient with alteplase-locked central venous catheter

Received: 5 August 2005 / Accepted: 5 August 2005 / Published online: 3 December 2005

Abstract Alteplase has been shown to be effective in preventing central venous access clotting in patients on hemodialysis. Because of a high phosphorus content in its excipient, it can inadvertently contaminate blood samples, leading the physician in care of the patient to erroneously increase dialysis time or change diet in order to control the pseudo-hyperphosphatemia.

Keywords Alteplase · Chronic kidney disease · Hemodialysis · Hyperphosphatemia · Phosphate

Sirs,

Vascular access remains a major problem in patients with chronic kidney disease on hemodialysis, because of the very high frequency of complications such as catheter-related infections or thrombosis [1]. To prevent clotting during the inter-dialysis period, highly concentrated heparin has been routinely used, with diverse success rates. Urokinase or recombinant tissular plasminogen activator (rt-PA) have traditionally been used as thrombolytic agents for hemodialysis vascular access declotting [2]. More recently, rt-PA has also been used instead of heparin to prevent catheter occlusion, and several studies have shown rt-PA to be superior to heparin in regard to catheter flow and pressure performances and clot weight [3, 4]. Because of the very high content of phosphorus in Actilyse (Boehringer Ingelheim, Basel, Switzerland), contamination of blood samples taken through the central venous catheter is possible, if rt-PA has not been removed sufficiently. We here report the occurrence of surreptitious elevated phosphorus levels in a child because of the high phosphate content of rt-PA contaminating the blood sample.

A 3-year-old patient suffering from end-stage kidney disease has been dialyzed 3.5 h, three times a week, without any problems for several months. Because of poor blood flow through his central venous catheter, we recently used Actilyse instead of heparin to lock his catheter during the inter-dialytic period, which markedly improved his catheter blood flow. Shortly after, we noticed very high and fluctuating phosphorus levels before dialysis. The patient's mother said she had not modified his diet, and the dialysis nurse used the same routine, removing and discarding the first 2–3 ml of blood in the central venous catheter before taking blood for chemical analysis. The child was not getting phosphate-containing drugs [5]. Because the occurrence of sometimes extreme hyperphosphatemia could not be explained by diet or poor dialysis performance, we questioned the reliability of the phosphorus analysis and considered possible contamination with Actilyse and the phosphoric acid used as an excipient. Several simultaneous phosphorus measurements by the central line and in periphery showed striking differences in the phosphorus content, varying greatly from sample to sample (Table 1). Each vial of Actilyse contains 107.2 mg of phosphoric acid for 10 mg of Actilyse. When reconstituted with sterile water, this gives a concentration of 109 mmol/l. An analysis of the reconstituted Actilyse (10 mg in 10 ml sterile water) showed a phosphorus concentration of 111 mmol/l (the other analysis being the following: sodium <0.5 mmol/l, potassium <0.1 mmol/l, chloride <10 mmol/l, calcium <0.1 mmol/l, and total proteins <2 g/l).

Because of its properties, phosphorus is extensively used in the pharmaceutical industry as buffering agent [6], as is the case with Actilyse. In the case of improper

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Table 1 Several simultaneous phosphorus measurements (in mmol/l) by the central line and in periphery showed striking differences in phosphorus content, varying greatly from sample to sample

Sample	Central line sample	Peripheral blood sample
1	6.14	2.21
2	2.77	1.39
3	7.18	1.81

rinsing of the catheter, contamination of the blood sample is very likely to occur. This can have dramatic consequences (change in diet, increasing the length of dialysis) in patients with chronic kidney disease on dialysis. After ruling out other causes of pseudo-hyperphosphatemia such as sample contamination with heparinized saline [7] or interference with paraproteins or hyperlipidemia [8, 9, 10], clinicians, and especially nephrologists, should be aware of this possible contamination of blood samples with phosphate due to improper rinsing when using phosphate-containing rt-PA such as Actilyse. A volume of blood equal to twice the dead volume of the indwelling line should be discarded before drawing blood for non-coagulation tests, in order to avoid interference with the drug left in place.

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