Intensive Care Med (2012) 38:1904–1905
DOI 10.1007/s00134-012-2653-6



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# Severe hyperkalemia in critically ill patients treated with prophylactic doses of enoxaparin

Accepted: 27 June 2012
Published online: 8 August 2012


Dear Editor,

Low-molecular-weight heparin (LMWH) is extensively used in intensive care unit (ICU) patients for prevention of thrombosis, with few adverse effects [1]. We report three cases of severe hyperkalemia induced by prophylactic doses of enoxaparin.

A 71-year-old diabetic man was admitted for sepsis, with creatinine and serum potassium concentrations of 1.5 mg/dL and 2.0 mEq/L. Potassium increased to 4.7 mEq/L with 60 mEq/day supplement. On day 4, potassium supplement was stopped and enoxaparin started [40 mg subcutaneously (SC) once daily (o.d.)]. By day 6, potassium had increased to 6.1 mEq/L and was resistant to insulin/dextrose and sodium polystyrene sulfonate (SPS) treatments. Enoxaparin was discontinued, and potassium decreased in 4 days. A few days later, enoxaparin (20 mg o.d.) was reintroduced and potassium increased to 5.2 mEq/L. The patient was treated with SPS and discharged without thrombosis prophylaxis (Fig. 1a).

A 63-year-old diabetic woman was admitted with cardiogenic shock. Creatinine was 0.7 mg/dL. Enoxaparin 20 mg o.d. was started and increased to 40 mg o.d. after 4 days. Serum potassium increased to 6.1 mEq/L within 3 days. The hyperkalemia was resistant to SPS treatment, and enoxaparin was withdrawn, following which there was a decrease in the potassium level. A few days later, enoxaparin was reintroduced and potassium increased again to 5.3 mEq/L rapidly. Enoxaparin was switched to fondaparinux (2.5 mg o.d.), and the potassium returned to normal values (Fig. 1b).

A 71-year-old woman, treated for arterial hypertension, was admitted for spinal cord injury. Her creatinine concentration was 0.4 mg/dL. Five days after surgery, enoxaparin (40 mg o.d.) was started. Potassium rapidly increased, needing treatment with SPS.

Enoxaparin was switched to fondaparinux (2.5 mg o.d.), resulting in a decrease in potassium to 4.6 mEq/L. A few days later,

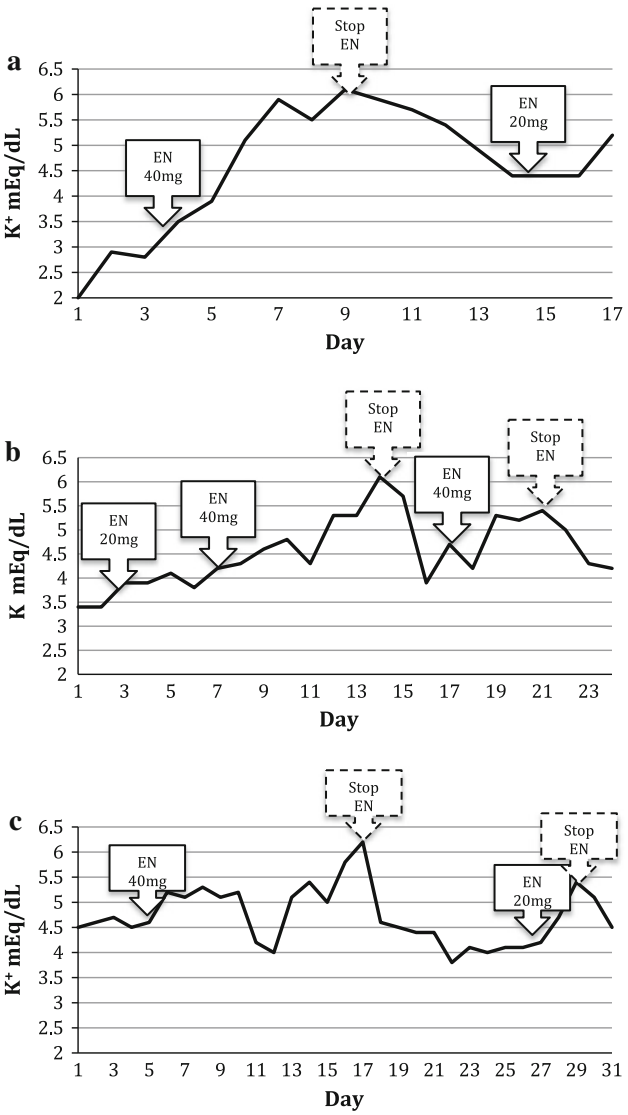


**Fig. 1** Evolution of serum $K^+$ level over time in the three patients. *EN* enoxaparin

enoxaparin (20 mg o.d.) was restarted and potassium increased again to 5.4 mEq/L. Fondaparinux was definitively used, and potassium returned to normal values (Fig. 1c).

These cases demonstrate that severe hyperkalemia can occur in association with prophylactic doses of enoxaparin. Hyperkalemia is a rare (2.4 %) [2] but well-documented side-effect of LMWH [3, 4]. Mechanisms involve inhibition of aldosterone by reduction in both the number and affinity of angiotensin II receptors in the zona glomerulosa, but an effect on aldosterone synthesis has also been suggested [5].

This effect is correlated with renal failure, diabetes mellitus, admission potassium level, and concomitant treatment with angiotensin-converting enzyme inhibitors [2–4], but can also occur in patients without risk factors, as in our three patients.

Hyperkalemia may be reversed by discontinuation of LMWH administration. If anticoagulation is needed, alternatives such as factor Xa inhibitors or direct thrombin inhibitors may be used [1]. Fludrocortisone has also been suggested [5].

Because of the widespread use of prophylactic enoxaparin in ICU patients, intensivists should be aware of this potentially life-threatening complication and monitor potassium levels during treatment even if patients have no risk factors for hyperkalemia.

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