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Case report

EXTREME HYPERKALAEMIA CAUSED BY CONCOMITANT USE OF A NSAID AND AN ACE INHIBITOR IN AN ELDERLY PATIENT

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Extreme hyperkalaemia is a life-threatening electrolyte disorder. It is relatively common in patients with severe renal insufficiency. This report describes a case of extreme hyperkalaemia caused by drugs in an 82-year-old female patient without severe renal insufficiency, who was successfully treated without haemodialysis. The patient had been treated for arterial hypertension and type 2 diabetes mellitus for 30 years. Over the last years she had been receiving enalapril and metformin. Three weeks before the admission to the hospital, she was receiving a non-steroidal anti-inflammatory drug (NSAID) because of the back pain. She was admitted to hospital due to a collapse and weakness in the limbs. Laboratory tests showed extreme hyperkalaemia, high blood sugar, metabolic acidosis, elevated serum creatinine and blood urea nitrogen (BUN), and a slightly elevated serum sodium. On ECG, we noticed typical signs of hyperkalaemia.
The patient was treated with a slow intravenous bolus of calcium gluconate and intravenous infusion of sodium chloride with insulin, glucose with insulin and sodium bicarbonte. After the treatment, all laboratory findings normalised together and the patient felt better. This case shows that physicians should be very careful when prescribing NSAIDs to elderly patients treated with drugs that affect renal function.

KEY WORDS: *arterial hypertension, chronic diseases, diabetes mellitus, diclofenac, enalapril, side effects*

Extreme hyperkalaemia is a serious life-threatening disorder, mostly provoked by excessive intake of potassium. It is most common in patients with severe chronic renal insufficiency and end-stage renal failure (ESRF), (1,2)

Drugs that lower elimination of renal potassium include potassium-sparing diuretics, cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) inhibitors, angiontensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) (2, 3). Patients with the history of renal impairment such as diabetic nephropathy, chronical glomerulonephritis, and impairment caused by long-lasting arterial hypertension (3) are more susceptible to the adverse effects of these drugs.

Here we report a case of extreme hyperkalaemia caused by concomitant treatment with a non-steroidal anti-inflammatory drug (NSAID) and an ACE Inhibitor in an elderly diabetic patient, who had not had a severe kidney disease.

CASE PRESENTATION

Our 82-year-old female patient was admitted to the emergency department because of vomiting, diarrhoea, and collapse. She could not stand and could

hardly move hands. For the last 30 years she had been treated for arterial hypertension and diabetes mellitus. Over the last couple of years she had been receiving enalapril 2x20 mg and metformin 3x850 mg. For three weeks before admission to the hospital, she had been taking diclofenac 2x50 mg because of the back pain. She started to feel weakness in the limbs a couple of days before admission.

On admission, we made urgent laboratory tests, which showed extremely high potassium level, high sugar, creatinine, blood urea nitrogen (BUN), sodium, and metabolic acidosis (Table 1). Electrocardiogram (ECG) showed typical signs of hyperkalaemia: high T waves in precordial leads, widened QRS complexes, and low P-waves.

At the emergency department, our patient immediately received a slow release bolus of intravenous calcium gluconate, after which she could move her limbs. We continued treatment with an infusion of 0.9 % sodium chloride and insulin, and when blood sugar dropped below 13 mmol L^{-1}, switched to infusion of glucose and insulin. To counter metabolic acidosis, the patient received infusion of sodium bicarbonate. We also made urgent echosonography of the kidneys and urinary tract, which did not show signs of renal insufficiency or urinary tract obstruction.

Our treatment normalised blood potassium and other laboratory tests without the need for haemodialysis, and the patient started to feel better. She was moved to the internal medicine ward, where she received an oral antihyperglycemic drug, a lower dose of enalapril and a calcium antagonist for hypertension. At the control visit, we made tests for serum cortisol, rennin, and aldosterone. None indicated hyporeninism/hypoaldosteronism or adrenal insufficiency.

DISCUSSION

Extreme hyperkalaemia needs immediate treatment that most often includes haemodialysis. Serum potassium level above 6.5 mmol L^{-1} brings the risk of fatal ventricular fibrillation and cardiac arrest (4). It is relatively common in dialysis and pre-dialysis patients

Table 1 *Laboratory findings in our 82-year-old female patient with severe hyperkalaemia*

Parameter	On admission	3 h later	12 h later	48 h later	30 days later	Reference intervals
Potassium / mmol L^{-1}	9.49	8.04	7.32	3.9	5.6	3.9 to 5.1
Sodium / mmol L^{-1}	130	134		141		137 to 146
Chloride / mmol L^{-1}	102	105		111		98 to 108
Calcium / mmol L^{-1}	2.21					2.14 to 2.53
Phosphate / mmol L^{-1}	1.95					0.75 to 1.42
Magnesium / mmol L^{-1}	0.78			0.82		0.5 to 1.05
Creatinine / mmol L^{-1}	159			90	107	79 to 125
Urea / mmol L^{-1}	13.82			6.15		2.8 to 8.3
C-reactive protein / mg L^{-1}	<5					
pH	7.27	7.31	7.40			7.35 to 7.45
Serum bicarbonate / mmol L^{-1}	15	18	24			23 to 27
Blood sugar / mmol L^{-1}	23.92	18	9	8	9	4.2 to 6.4
Troponin I / ng mL^{-1}	0.00					<0.3
Leukocytes / $x10^9$ L^{-1}	19.3			11.6		3.4 to 9.7
Hemoglobin / g L^{-1}	124			122	121	119 to 159
Thrombocytes / $x10^9$ L^{-1}	444			475		158 to 424
Aldosterone / pmol L^{-1}					480 (standing)	105 to 860 (standing) 80 to 400 (lying)
Plasma renin activity / µg L^{-1} h^{-1}					1.22 (standing)	0.5 to 1.9 (standing) 1.9 to 6.0 (lying)
Cortisol / nmol L^{-1}					290 (8 h am)	138 to 800 (8 h am) 80 to 480 (5 h pm)

with ESRF who have taken too much potassium with food and drink (1, 2). The ECG of our patient showed typical signs of hyperkalaemia.

ACE inhibitors are widely used for arterial hypertension. Together with angiotensin II receptor blockers (ARB) they lower blood pressure and renal perfusion, decreasing the burden of glomerular filtration.

They also owe their renoprotective and cardioprotective effect to inhibition of the growth factors and to the lowering of oxidative stress, which are associated with chronic changes in the kidneys, heart, and blood vessels (5, 6).

ACE inhibitors affect the renin-angiotensin-aldosterone system and lower potassium elimination through the kidney, especially in patients with diabetes, hypertension, and in elderly patients (7). In addition to chronic treatment with ACE inhibitor, our patient was prescribed a NSAID because of the back pain. Renal side effects of NSAIDs are common (seen in up to 5 % patients). These include acute kidney injury, acute interstitial nephritis with nephrotic syndrome, electrolyte and fluid disorders, hypertension, and analgesic nephropathy. Similar side effects are seen in patients using inhibitors of COX-1 and COX-2. The most common side effect of NSAIDs, especially in patients at risk, is acute kidney injury with retention of water, sodium, and potassium, resulting in hyperkalaemia (8). In our patient, hyperkalaemia was the consequence of interaction between the ACE inhibitor and the NSAID during concomitant administration. NSAID led to a gradual increase in the potassium level, acidosis, and renal failure. NSAIDs are prostaglandin synthesis inhibitors and affect renal blood circulation. They can cause acute renal failure by critically reducing renal flow. NSAIDs induce hyporeninemic hypoaldosteronism, which underlies hyperkalaemia and non-gap metabolic acidosis (8-10). As we did not test for renin and aldosteron while diclofenac was still acting on the renin-angiotensin system, we have no laboratory confirmation of hyporeninemic hypoaldosteronism. Viral gastroenterocolitis with vomiting and diarrhoea could cause a mild dehydration and lowering of renal perfusion. Vomiting, in turn, could have been caused by hyperkalaemia with acidosis. Insulin deficiency with hyperglycaemia could also have contributed to hyperkalaemia (2, 11).

The highest reported hyperkalaemia with cardiac arrest and successful resuscitation was 14 mmol L^{-1} (12). Other authors reported hyperkalaemia of 9.3 mmol L^{-1} with lethal outcome (13, 14). Patel et al. reported a similar case of quadriparesis in a hyperkalaemic patient with metabolic acidosis, who was previously treated with diclofenac, but the patient had a lower level of potassium (15). Hyperkalaemia in elderly patients has more often been observed since new treatment recommendations for chronic heart failure have been adopted and new drugs introduced for other diseases (16).

We did not find evidence of any other cause of hyperkalaemia. The patient did not take other potassium-raising drugs such as potassium-sparing diuretics, beta blockers, or digitalis. The level of plasma cortisol was also normal. There were no signs of hypercatabolism such as body injury or massive haemolysis.

As elderly people often suffer from arterial hypertension and musculoskeletal pain, they are prescribed ACE inhibitors and NSAIDs. Because of possible interactions, physicians should be very careful when prescribing these drugs, especially in diabetic patients and patients with a kidney disease, and are strongly advised to often run control laboratory tests, especially for serum potassium and creatinine.

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Sažetak

EKSTREMNA HIPERKALEMIJA U STARIJE BOLESNICE UZROKOVANA NESTEROIDNIM ANTIREUMATIKOM I ACE-INHIBITOROM

Ekstremna hiperkalemija je za život opasan poremećaj elektrolita. Relativno je česta u bolesnika s teškim bubrežnim zatajivanjem. Ovaj prikaz opisuje slučaj ekstremne hiperkalemije uzrokovane lijekovima u 82-godišnje bolesnice bez težega bubrežnog zatajivanja, a koja je bila uspješno liječena bez hemodijalize. Bolesnica je unatrag 30 godina bila liječena zbog povišenoga krvnog tlaka i šećerne bolesti. Zbog arterijske hipertenzije uzimala je enalapril, a zbog šećerne bolesti metformin. Tri tjedna prije hospitalizacije uzimala je nesteroidni antireumatik zbog bolova u leđima. Bolesnica je bila primljena u bolnicu nakon što je kolabirala uz osjećaj izrazite slabosti u udovima. U laboratorijskim nalazima bile su prisutne ekstremna hiperkalemija, hiperglikemija, metabolička acidoza, povišene razine serumskog kreatinina i ureje te blago povišena vrijednost serumskog natrija. Na EKG-u su bili registrirani tipični znakovi hiperkalemije. Bolesnica je bila liječena polaganim bolusom kalcijeva glukonata, intravenskim infuzijama natrijeva klorida uz inzulin, otopinom glukoze uz inzulin i otopinom natrijeva bikarbonata. Liječenjem su se laboratorijski nalazi normalizirali uz poboljšanje subjektivnoga stanja bolesnice. Ovaj prikaz upozorava na to da liječnici moraju biti vrlo oprezni pri propisivanju nesteroidnih antireumatika starijim bolesnicima liječenima lijekovima koji mogu utjecati na bubrežnu funkciju.

KLJUČNE RIJEČI: *arterijska hipertenzija, diklofenak, enalapril, kronične bolesti, nuspojave, šećerna bolest*

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