Case study
DOI: 10.19271/IRONS-000159-2022-38

Pozaszpitalne zatrzymanie krążenia wywołane hipokaliemią – opis przypadku

Streszczenie

Zagrażające życiu zaburzenia elektrolitowe, takie jak nagłe zmiany stężenia potasu w osoczu mogą spowodować lub prowadzić do poważnych zaburzeń kardiologicznych, w tym do zatrzymania krążenia.

Prezentowana praca przedstawia przypadek 57-letniego pacjenta z hipokaliemią o niejasnej etiologii, który przy wysiłku fizycznym doświadczył pozaszpitalnego zatrzymania krążenia (ang. out-of-hospital cardiac arrest, OHCA). Czynności reanimacyjne zostały zainicjowane natychmiastowo przez świadka zdarzenia i kontynuowane przez Zespół Ratownictwa Medycznego. Wskutek skutecznej resuscytacji i defibrylacji uzyskano powrót spontanicznego krążenia, niemniej pacjent pozostał w śpiączce przez następne cztery dni. Poza łagodnym nadciśnieniem tętniczym leczonym kombinacją walsartanu (antagonista receptora AT1 angiotensyny II) i hydrochlorotiazydu, pacjent nie posiadał innych chorób współistniejących. Przy przyjęciu: rytm zatokowy miarowy 80/min, stężenie potasu 2.8 mmol/l, Glasgow Coma Scale 3, ciśnienie tętnicze w normie. Angiografia wieńcowa nie wykazała niedrożności naczyń wieńcowych. Pozostałe dodatkowe badania także nie wykazały zmian.

Po wybudzeniu pacjent z zaburzeniami świadomości i pamięci. W 14. dobie hospitalizacji pacjent stabilny krążeniowo, chodzący przy pomocy pielęgniarki został wypisany do domu. Siedemnaście miesięcy później u pacjenta nadal występuje ciężkie upośledzenie funkcji poznawczych, brak motywacji, osłabienie mięśni i zmęczenie. Pacjent wymaga specjalnej opieki, w tym nadzoru i pomocy w codziennych czynnościach.

W ustaleniu przyczyn hipokaliemii, które nie zostały jednoznacznie zdefiniowane wzięto pod uwagę kilka potencjalnych patomechanizmów.

Słowa kluczowe: OHCA, zatrzymanie krążenia, hipokaliemia, zaburzenia elektrolitowe

---

Hypokalemia - induced out-of-hospital cardiac arrest - case study

Bartłomiej J. Czyżniewski[1], Iga Kolasa[1]*, Magdalena Gibas-Dorna[2]

[1] Students' Scientific Society, Collegium Medicum, University of Zielona Góra, Poland

[2]Department of Applied and Clinical Physiology, Collegium Medicum, University of Zielona Góra, Poland

Abstract

Life-threatening electrolyte abnormalities, such as sudden changes in serum potassium cause or contribute to fatal cardiac consequences, including cardiac arrest.

Here we present a case of 57-year-old man with unrecognized hypokalaemia who experienced exercise-related out-of-hospital cardiac arrest (OHCA). Successful CPR was initiated immediately, however he remained in a coma for a four days. The patient had no other comorbidities, except from a history of mild hypertension treated with low doses of angiotensin receptor blocker (ARB) combined with thiazide. On admission: sinus heart rhythm 80 bpm, potassium level 2.8 mmol/l, Glasgow Coma Scale 3, blood

pressure normal. Coronary angiography did not show any coronary occlusion. Other additional tests were nonspecific.
Upon awakening, he had a major confusion with severe memory deficits. A week later, he was able to walk and was discharged from the hospital.
Seventeen months later the patient still struggles with severe cognitive impairment, lack of motivation, muscle weakness, and fatigue. He requires special care, including supervision and help with activities of daily living.
Although the exact cause of hypokalaemia remained unrecognized, several probable mechanisms were taken into consideration.

Keywords: OHCA, cardiac arrest, hypokalaemia, electrolyte disturbances

---

Corresponding author:
Bartłomiej J. Czyżniewski
Students' Scientific Society
Collegium Medicum
University of Zielona Góra
28 Zyty Street
65-046 Zielona Góra
Poland
e-mail address: bartlomiejczyzniewski@gmail.com

Authors reported no source of fundin
Authors declared no conflict of interest

Date received: 24th July 2021

Date accepted: 25th August 2021

Introduction

OHCA *(out of hospital cardiac arrest*) is a sudden loss of mechanical activity of the heart. The patient may not be breathing or have agonal breath. The pulse may be not palpable and the patient may not react to stimuli. The causes of OHCA can be divided into cardiac and non-cardiac causes. Acute myocardial infarction, myocarditis, and cardiomyopathy are examples of cardiac causes. Trauma, hypoglycaemia, and hyperkalaemia are noncardiac causes of OHCA (Myat *et al.* 2018). One-third of patients with OHCA have no prior recognized heart disease, half of them have no prodromal symptoms (McCarthy James *et.al* 2018). The difference in membrane resting potential depends on internal and external potassium levels. Potassium ions take part in membrane potential formation. Because of that, K+ ions influence nerve and muscle cell excitability (Uruski and Tykarski 2009). Even little disturbances of potassium homeostasis may have major consequences.

Electrolyte abnormalities, including hyper- and hypokalaemia, may generate life threating arrhythmias leading to cardiac arrest, particularly in the setting of preexisting structural cardiac abnormalities. Although occurrence of hypokalaemia is more prevalent than hyperkalaemia in clinical practice, most cases of low potassium levels are mild, ranging from 3.0 to 3.4 mmol/L and might not cause symptoms (Castro and Sharma 2021).

Hormones like insulin or aldosterone, influence potassium homeostasis also. They increase potassium transport to the intracellular space via a cellular membrane. It appears that clinically relevant hypokalaemia is not widespread and usually results from rapid and/or severe gastrointestinal or renal losses, including uncontrolled for potassium level use of diuretics, hyperreninism and hyperaldosteronism (Castro and Sharma 2021; Ferreira JP *et al.* 2020). Although in most patients the cause of K+ depletion is clearly indicated by the patient's history (eg., vomiting or diarrhoea, diuretics), there are episodes of unrecognised origin which contribute significantly to the incidence of cardiac arrhythmias and high risk of mortality. Common causes of hyperkalaemia are pharmacotherapy and renal insufficiency (Manitius 2011). Some

patients with chronic kidney disease which also have diabetes as a consequence, may develop hyporeninemic hypoaldosteronism. The lack of aldosterone usually leads to increase retention of potassium ions and as a consequence to hyperkalaemia. Some authors also detail pseudohypokalaemia – for example, in patients with leukocytosis or when haemolysis appears in unspin blood samples (Kokot *et. al* 2006). When blood is taken for the tests after 20-30 minutes from insulin injection in the patient, pseudohypokalaemia could appear too (Manitius 2011).

The aim of our paper is to present a hypokalaemia-induced case of OHCA in a patient without a significant burden of cardiovascular diseases and to identify the most probable cause factors that explain the pathophysiological approach.

Case

A 57-year-old man, with a history of mild hypertension, collapsed while playing basketball with friends. He lost consciousness, stopped breathing, and his pulse was impalpable. Cardiopulmonary resuscitation (CPR) was initiated immediately by his son and continued until emergency medical staff (EMS) arrived. The EMS found him in cardiopulmonary arrest. An automated external defibrillator (AED) detected a ventricular fibrillation (VF)-like waveform and an electrical shock was administrated at 150 joules. Fifteen minutes after collapse he arrived to the nearest intensive care unit (ICU) for further treatment. On admission, the patient was areflective (3 points in Glasgow Coma Scale), his heart rhythm was sinus rhythm with premature ventricular beats, blood pressure was normal. Following admission to ICU, he was intubated and ventilated artificially. His blood results revealed clinically relevant hypokalaemia (serum potassium level 2,85 mmol/L) and high troponins (troponin T hs = 1097 ng/L). Brain CT scan was normal with no detectable signs of bleeding, hematoma, injury, ischemia, or any other pathology. Chest CT showed mild bilateral pneumonia and no other abnormalities. Coronary angiography demonstrated no significant coronary artery stenosis and echocardiography showed normokinesis, left ventricular ejection *fraction* 65%, mild hypertrophy of left ventricular wall and normal valvular morphology & dynamics. In 24-h ECG analysis, sinus heart rhythm was detected with low variability and the N-N interval (SDNN) of 58. Abdominal sonography showed hypoechoic structure next to the lower pole of left kidney which was diagnosed as an additional kidney. The patient remained in coma for four days. Ice cube bags were used superficially to lower patient's head temperature. Upon awakening and extubation, he had a major confusion with severe memory deficits and demonstrated slight hand tremor and lowered muscle tone. Severity of cognitive impairment was derived from behavioural observation and clinical interviews. On day 11th, the patient was able to walk with an assistance, three days later he was discharged from hospital. After five months, he was referred to the Clinic of Endocrinology for further examination, but no significant hormonal abnormalities were found.

Although the exact cause of hypokalaemia remained unrecognized, several probable mechanisms were taken into consideration.

Hyperaldosteronism

Aldosterone, is one of the three components of the renin–angiotensin system (RAS) which regulates the blood pressure, fluid, and electrolyte balance. It acts on the late distal tubule and collecting duct of nephrons causing sodium absorption from the lumen and potassium excretion into the urine. According to the retrospective observational study conducted by Burrello et al., the main causes of hypokalaemia in patients with essential hypertension were diuretic therapy or primary aldosteronism (Burello *et al.* 2020). Aldosteronism is caused by either a primary tumour capable of secreting extra

aldosterone within the adrenal zona glomerulosa, or by renovascular hypertension. In this case, the patient was referred to the Clinic of Endocrinology to determine whether RAS was affected. Interestingly, abdominal ultrasound scan revealed a hypoechogenic structure (4 cm of length) localised next to the lower pole of the left kidney, which was described (without further interpretation) as a third supernumerary kidney. A single-photon emission computerized tomography (SPECT) showed a small thickening in the lower part of the left adrenal (10x8 mm) with a radio density of 16 Hounsfield Units (HU), however, CT scan did not confirm any abnormality. Moreover, blood criteria for hyperaldosteronism were negative: both supine plasma levels of renin and aldosterone (5.57 uIU/ml and 16,80 ng/ml, for renin and aldosterone respectively) as well as after verticalization (9.43 uIU/ml and 20.90 ng/ml, for renin and aldosterone respectively) were normal. Changes in plasma renin and aldosterone in the salt loading test (SLT) measured after intravenous infusion of 2 L of sodium chloride 0.9% over 4 hours, were also within normal range (renin dropped from 5.34 to 2.14 uIU/ml and aldosterone from 14.70 to 7.89 ng/ml).

In summary, based on hormonal examination, the most prevalent endocrine reason for hypokalemia can be ruled out.

Diuretics

As stated by all major guideline committees, diuretics should be used as an initial therapy for most hypertensive patients, because they reduce cardiovascular mortality and morbidity caused by hypertension. These drugs belong to a large group of antihypertensive agents that may contribute to blood potassium level. Thiazides and loop diuretics are known to decrease blood potassium concentration. Although thiazide-type diuretics indirectly stimulate K+ secretion by the renal distal tubule, little evidence exists for the association between mild diuretic-induced hypokalaemia and cardiac arrhythmias in the absence of underlying heart disease (Papademetriou 2006). Nevertheless, some authors suggest a need to prevent thiazide-induced potassium depletion by lowering the dose of a drug, oral K+ supplementation, or adding a potassium-sparing diuretic drug when higher diuretic doses are needed (Grobbee and Hoes 1995).

In the present case, the patient had a history of mild essential hypertension treated with a small dose of Co-bespres, which combines thiazide and angiotensin II type 1 receptor blocker (ARB). By blocking angiotensin II binding to the adrenal receptor on zona glomerulosa cells, ARB inhibits normal aldosterone secretion, which in turn, impairs kidney excretion of potassium. Thus, ARB acts as a potassium-sparing diuretic and may balance hypokalemic effects of thiazide. Knowing that potassium-lowering effect of thiazide is dose-dependent (Carlsen *et al.* 1990), using low doses of these antihypertensive drugs is relatively safe, particularly in patients with no other cardiac dysfunction (Mukete and Rosendorff 2013).

Taken together, a low dose of thiazide combined with potassium-sparing ARB (12,5 mg of Hydrochlorothiazide/80 mg of Valsartan daily) and the absence of any serious heart muscle dysfunction are less likely to evoke clinically relevant hypokalaemia with K+ concentration less than 3,0 mmol/L. However, this effect may occur when the other predisposing factor is present and when the baseline blood potassium concentration is low or low-normal.

Blood potassium shifts during exercise

There are two general types of regulatory mechanisms involved in potassium homeostasis. Long-term regulation, that is mainly due to K+ excretion by kidneys and short-term regulation, which occurs within seconds to minutes and involves, to a large

extend, the skeletal muscle pool of potassium (Kjeldsen and Schmidt 2019). Physical activity with repetitive action potentials that occur across myocyte membranes is associated with the release of large amounts of K+ from contracting skeletal muscle. Moreover, due to the exercise-evoked haemoconcentration, which is caused by shift of fluid from plasma into an interstitial and intracellular compartments, blood potassium is additionally elevated (Lindinger and Sjøgaard 1991). During repeated bouts of exercise and generation of action potentials, the efficiency of muscular sodium-potassium pumps to pump back the same amount of K+ that was lost with repolarizing K+ currents, appears to be insufficient. Consequently, physiological hyperkalaemia with the peak postexercise plasma K+ concentration around average value of 8.0 mmol/L is observed, and plasma K+ increases linearly with intensity and exponentially with the duration of physical activity (Medbø and Sejersted 1990). Such a high plasma potassium is closely related to muscle fatigue and exercise cessation, preventing from further K+ rise to toxic levels (Lindinger and Sjøgaard 1991). In addition, it seems that right after exercise cessation, the sympathetic drive with high catecholamines may contribute to increased sodium-potassium pump efficiency, possibly by raising the pump's sensitivity to elevated intracellular sodium concentration, which initiates rapid K+ fall (Medbø and Sejersted 1990). The muscular pumping capacity also depends on other factors at onset of exercise, such as an adequate ATP supply, hormonal control other than catecholamines, Na+-K+ pump density in skeletal muscle cells and others. When the abundance of active Na+-K+ pumps is high, the half-time for recovery of K+ after exercise is shorter, which occurs particularly after the dynamic type of exercise, when activated muscle mass is large, and in individuals with high physical activity level (Sejersted and Sjøgaard 2000). The transient, postexercise reduction of blood K+ to below normal resting values may last several minutes leading to postexercise hypokalemia. Hence, the combination of exercise-evoked potassium fluctuations together with raised catocholamines and previously unrecognized low potassium levels may evoke seriously dangerous tachyarrhythmia leading to cardiac arrest (Skogestad and Aronsen 2018).

Here we assume that in the present case of OHCA, exercise could possibly work as a trigger of hypokalemia and ventricular fibrillation.

At present

The patient still struggles with memory and cognitive problems. Lowered muscle mass, fatigue, and mild depression have a significant impact and negatively affect his daily functioning. He requires special care, including supervision and help with activities of daily living. Given that OHCA survivors are at high risk of long-term cognitive impairment, patients should follow both individualized cardiac and neurological rehabilitation, however, the combined cardiac and cognitive program for OHCA survivors in Poland is not routinely assessed upon discharge and not refundable through the National Health Fund. Therefore, family members initiative and support is the only way to provide care, supervision, and coordination of the rehabilitation process, which includes everyday moderate physical activity, board games, and other activities to stimulate cognition and memory, biofeedback training, private neuropsychologist visits, brain neurostimulation therapy. However, due to lockdown and travel restrictions, COVID-19 pandemic limits the possibilities for intense rehabilitation.

Conclusions

1. To reduce the risk of fatal cardiac arrhythmia evoked by exercise, the use of thiazides in combination with ARBs necessitates routine blood testing for potassium.
2. Establishing specialized neurorehabilitation centres is essential for treating OHCA

survivors with cognitive and memory deficits.
3. Individualized neuro-rehabilitation should be implemented routinely for patients with cognitive problems and dementia.
4. Due to pandemic disruption of healthcare systems, OHCA survivors may have worse long-term outcomes.

REFERENCES

Burrello J., Monticone S., Losano I., Cavaglià G., Buffolo F., Tetti M., Covella M., Rabbia F., Veglio F., Pasini B., Williams T.A., Mulatero P.(2020) *'Prevalence of Hypokalemia and Primary Aldosteronism in 5100 Patients Referred to a Tertiary Hypertension Unit*.' Hypertension, 75(4) pp. 1025-1033.

Carlsen J.E., Kober L., Torp-Pedersen C., Johansen P.(1990) *'Relation between dose of bendrofluazide, antihypertensive effect, and adverse bio-chemical effects.'* BMJ; 300 pp. 975–978.

Castro D., Sharma S. (2020) *'Hypokalemia'*, In: StatPearls. StatPearls Publishing, Treasure Island (FL).

Ferreira J.P., Butler J., Rossignol P., Pitt B., Anker S.D., Kosiborod M., Lund L.H., Bakris G.L., Weir M.R., Zannad F.(2020) *'Abnormalities of Potassium in Heart Failure: JACC State-of-the-Art Review.'* J Am Coll Cardiol. 75 (22)pp. 2836–2850.

Kokot F., Kokot F., Kokot E. (2006)*. "Hipokaliemia."* Choroby Serca i Naczyń 3.4): pp. 203-206.

Grobbee D.E., Hoes A.W. (1995) *'Non–potassium-sparing diuretics and risk of sudden cardiac death'.* J Hypertens.; (12 Pt 2): (13) pp. 1539- 1545.

Kjeldsen K.P., Schmidt T.A. (2019) *'Potassium homoeostasis and pathophysiology of hyperkalaemia.'* Eur Heart J Suppl, (Suppl A): A2–A 5.

Lindinger M.I., Sjøgaard G. (1991) '*Potassium regulation during exercise and recovery.*' Sports Med. (6) pp. 382-401.

Manitius J. (2011) '*Hiperkaliemia i hipokaliemia.'* Forum Nefrologiczne 2011, vol. 4, no 4, pp. 367–372.

McCarthy J.J., Carr B., Sasson C., Bobrow B.J., Callaway C.W., Neumar R.W., Ferrer J.M.E., Garvey J.L., Ornato J.P., Gonzales L., Granger C.B., Kleinman M.E., Bjerke C., Nichol G. (2018) *'Out-of-hospital cardiac arrest resuscitation systems of care: a scientific statement from the American Heart Association.*' Circulation (137.21)pp. 645-660.

Medbø J.I., Sejersted O.M. (1990) *'Plasma potassium changes with high intensity exercise.'* J Physiol. (421)pp. 105-122.

Mukete B.N., Rosendorff C. (2013) Effects of low-dose thiazide diuretics on fasting plasma glucose and serum potassium-a meta-analysis. J Am Soc Hypertens. (6), pp. 454-66.

Myat A., Song K.J., & Rea T. (2018). '*Out-of-hospital cardiac arrest: current concepts.*' The Lancet, 391(10124) pp. 970-979.

Papademetriou V. (2006) '*Diuretics, hypokalemia, and cardiac arrhythmia: a 20-year controversy*'. J Clin Hypertens (Greenwich) 8(2)pp. 86-92.

Sejersted O.M., Sjøgaard G. (2000) '*Dynamics and consequences of potassium shifts in skeletal muscle and heart during exercise.*' Physiol Rev. 80(4) pp. 1411-81

Skogestad J., Aronsen J.M. (2018) *'Hypokalemia-Induced Arrhythmias and Heart Failure: New Insights and Implications for Therapy.'* Front Physiol.;9:p.1500.

Uruski P.,Tykarski A. (2009). *'Znaczenie i zasady kontroli gospodarki potasowej w chorobach sercowo-naczyniowych.'* Forum Medycyny Rodzinnej. Vol. 3. No.1 pp.49-60.