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Emergency treatment of excessive hyperkaliemia with ominous ECG-signs

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1. Abstract

Potassium is mainly eliminated through the kidneys and accumulates when the renal function falls below 25 % of normal level. Medication and disease may trigger aggravation or the origin of renal failure. If renal failure progresses unnoticed, severe hyperkaliemia may be the result and lead to fatal arrhythmias. Two cases of excessive hyperkaliemia approximately 10 mmol/L are reported and etiologies, symptoms, ominous ECG-signs and treatments are reviewed. Among other things, these patients were being treated for systolic heart failure, hypertension and diabetes with ACE-I, ARB, MRA, BB, Digoxin and Metformin. In the first case, renal failure resulted from addition of NSAID and in the second case from dehydrating diarrhea. Both patients received emergency treatment with Calcium Chloride, Insulin-Glucose, Salbutamol and Hemodialysis and their lives were saved.

2. Keywords: Excessive hyperkaliemia; Ominous ECG-signs; Emergency treatment; Case reports; Review

3. Abbreviations: ACE-I: Angiotensin-Converting Enzyme Inhibitor; MRA: Mineralocorticoid Receptor Antagonist; ARB: Angiotensin Receptor Blocker; BB: Beta Blockers; NSAID: Non-Steroidal Anti-Inflammatory Drug; RAAS: Renin-Angiotensin-Aldosterone System; IV: Intravenously

4. Introduction

Excessive hyperkaliemia (>9 mmol/L) is associated with high mortality and S-K >10 mmol/L is considered inconsistent with life due to myocardial instability and fatal arrhythmias. Hyperkaliemia can be very challenging to diagnose, but fast recognition of this fatal condition and swift and appropriate treatment may be lifesaving and should be known by heart.

However, outcome is not only determined by the serum concentration of potassium. It also depends on baseline ECG, diverse comorbidities, cotreatments and comedications and whether hyperkaliemia is acute or chronic as rapid increase in S-K is more dangerous than slow increase leaving time to adapt [1,2]. Fast infusion of potassium brings about cardiac arrhythmias and stops the heart. This is utilized in legalized euthanasia and when executing the death penalty.

The cell membrane potential depends on an equilibrium state created by the Na^+/K^+-ATPase in the concentration of Na^+ and K^+ inside and outside the cell. As 98% of the potassium in the body is intracellular, even small changes in the extracellular concentration may influence the membrane potential and change the depolarization and the repolarization thereby leading to changes in the ECG, and serious arrhythmias [3,4].

Prompt analysis of the cause of excessive hyperkaliemia and the resulting intervention and treatment, including dialysis, may be lifesaving as in the two cases of extreme

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two cases of extreme hyperkaliemia presented here and illustrated with typical and ominous ECG-changes.

5. Case Presentation 1

A 67-year old male was taken urgently from his home to the emergency department at the hospital. He was soporous and reacted to pain, he was breathing 33 times/min. with cyanosis and O_2-saturation 80%, he was dehydrated, cold, contracted, and clammy with blood pressure 80 mm Hg/40 mm Hg, pulse 30 bpm, and core temperature 34ºC.

S-K was immeasurable in three consecutive ABL-tests meaning S-K>8 mmol/L, S-creatinine 474 micromole/L, GFR 10, S-carbamid 30 mmol/L, pH 7, base excess -15, S-hydrogencarbonate 11 mmol/L, S-lactate 4.7 mmol/L, P-glucose 10 mmol/L, leucocytes 20 x 10E9/L, CRP 36 mg/L. Normal echocardiography, EF 60%.

ECG showed absence of P-waves, sinoatrial block, and an irregular and slow rhythm with broad QRS-complexes changing into sine waves.

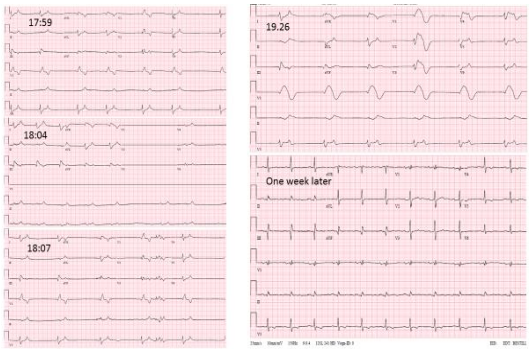

Figure 1: ECG showing ominous changes due to hyperkaliemia approximately 10 mmol/L. Sine waves at 19:26 (7:26 PM) are warnings of imminent heart stop. After normalization of S-K, the ECG returned to the usual baseline ECG, illustrated one week later.

He was administered Normal Saline, Human Albumin, Ephedrine, Atropine, Isoprenaline, Noradrenaline, Piperacillin-Tazobactam, and 100 mL of 8.4% Bicarbonate due to the severe metabolic acidosis.

While he was treated for hyperkaliemia according to Table 1, a S-K value of 9.3 mmol/L was measured using another analyser. Due to recurrent episodes of asystolia, it was decided to implant an external pacemaker and he was subsequently paced 70 bpm in the right ventricle with capture at 1.2 V. In addition to this, he also had a HD-catheter implanted and immediately went on to have hemodialysis performed.

Clinically and biochemically he improved within a few hours. He started to have diuresis, S-K and S-lactate normalized, and the renal function improved and finally normalized. He remained disoriented until the next day, when he was sufficiently able to tell his story.

He had a history of (i) ischemic heart disease with prior myocardial infarction, Q-waves in the inferior leads, CABG, and heart failure treated with Enalapril 15 mg x 2 (ACE-I), Spironolactone 25 mg x 1 (MRA), Furosemide 40 mg x 1, Kaleorid 750 mg x 1, Metoprolol 50 mg x 1 (BB), Atorvastatin, and Clopidogrel; (ii) hypertension; (iii) apoplexia cerebri with cognitive deficits and dysfunction; (iv) NIDDM treated with Metformin 1 g x 2; (v) alcohol abuse and prior Wernicke's encephalopathy treated with Thiamin and B-Combin; (vi) smoking and COLD; (vii) sleep apnea treated with CPAP; and (viii) chronic back pain. He had last been to see his GP two years previously and at that time his blood tests were normal. Weight 82 kg and height 170 cm.

Lately he had experienced falls at home and due to increased back pain, he had treated himself with Ibumetin 600 mg x 3 (NSAID). He had become increasingly weak, dizzy, and unsteady, had been having trouble climbing the stairs, and had started to use a walker. Up until a few weeks prior to his emergency admission, he had been out about every day and had no problems walking or climbing stairs.

Upon admission, all medication was withdrawn. After recuperation, his blood pressure was regulated with Amlodipine. Following the emergency treatment, he continued to have episodes of sinus bradycardia 25 bpm and nine days after admission he had a permanent pacemaker implanted. The following day he was discharged to a nursing home. The ECG had returned to baseline (Figure 1), the blood tests were normal, and he was fine according to the circumstances.

6. Case Presentation 2

A 78-year old male was admitted to hospital due to general malaise, dizziness, and severe and universal

muscular weakness to such a degree that he had had trouble using his telephone calling for help in a weak voice. The muscular problems had evolved gradually after he had started having diarrhea a couple of weeks earlier. On his way to hospital, he was diagnosed with bradycardia 26 bpm and received 1 mg of atropine.

He had a history of (i) atrial fibrillation for many years and was treated with Marevan, Digoxin 0.1875 mg x 1, and Carvedilol 25 mg x 2 (BB); (ii) hypertension treated with Losartan comp. (100+12.5 mg) (ARB), Enalapril 20 mg x 2 (ACE-I), and Spironolactone 25 mg x 1 (MRA); and (iii) NIDDM treated with Metformin 1 g x 2. His weight was 110 kg and height 180 cm, he displayed normal biochemistry and normal echocardiography, apart from dilatation of the atriums, and had been agile up until this point.

In the emergency room, he was found to be pale, clammy, and dehydrated. He had a pulse of 30 bpm, blood pressure 95/50 mm Hg, and O_2-saturation 97%. All medication was withdrawn.

He had S-K 9.7 mmol/L and immediately had another test, which showed S-K 9.9 mmol/L. S-creatinine 368 micromoles/L, pH 7.2, base excess -10, S-hydrogencarbonate 16 mmol/L, INR 2.7, S-lactate 1.5 mmol/L, P-glucose 9 mmol/L, leucocytes 13.6 x 10E9/L, CRP<2,9 mg/L, S-digoxin 4.6 nanomol/L.

ECG showed a wide, complex, and slow idioventricular rhythm.

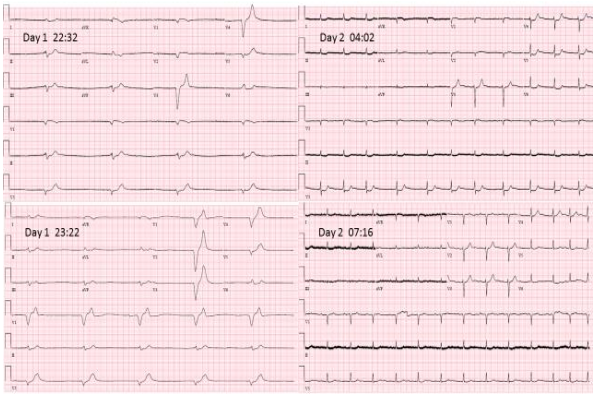

Figure 2: ECG day 1 with S-K approximately 10 mmol/L, and day 2 after normalization of S-K.

He was initially administered Atropine and Isoprenaline, 200 mL Bicarbonate 8.4%, Normal Saline and 40 mg of Furix intravenously (IV), 10 mL of Calcium Chloride IV, 50 mL of 50% Glucose with 10 IE Insulin and 1 liter 5% Glucose with 20 IU Insulin, and Salbutamol inhalation and IV (Table 1). Although his general condition improved markedly, his pulse remained at 30 bpm without the patient appearing notably affected, he was hemodynamically stable.

Emergency hemodialysis was performed without complications and resulted in sinus rhythm 60 bpm (Figure 2).

He subsequently improved clinically and biochemically (Table 2), converted back to atrial fibrillation and the usual baseline ECG (Figure 2), normalized S-K and renal function, and was discharged in good health and in stable condition after nine days in hospital.

7. Discussion

Often no specific clinical signs or symptoms are present to suggest even severe hyperkaliemia and clinicians must frequently rely on clinical information, laboratory data, and an array of insensitive nonspecific electrocardiographic changes to reach this diagnosis [3-6].

Total potassium levels are regulated mostly by the kidneys, with only 5%-10% of ingested potassium excreted in the feces [4,6]. Hyperkaliemia is usually the result of chronic renal failure and terminal uremia impairing the renal excretion of potassium [7]. Alternatively, it is multifactorial and often related to the medical treatment of systolic heart failure, hypertension, and diabetes mellitus [2,8], as in the two present cases.

Previously, both patients exhibited normal renal function, but they were treated with potentially nephrotoxic medications: An angiotensin-converting enzyme inhibitor (ACE-I) and a mineralocorticoid receptor antagonist (MRA) and in addition to this, patient 2 was administered an angiotensin receptor blocker (ARB).

These inhibitors of the renin-angiotensin-aldosterone system (RAAS) are important when treating patients with systolic heart failure, hypertension, and diabetes mellitus. Common side effects are reduced renal function and hyperkaliemia, observed especially in patients with renovascular disease and in the old and the elderly due to

the decline in renal function with age [3,7,9,10]. Due to the changing demography, which leads to increased occurrence of heart and kidney failure, problems with inhibitors of RAAS, side effects, renal failure, and hyperkaliemia are expected to increase markedly [3]. Monitoring potassium levels is important in at-risk patients receiving these medicines [7,10]. It is important to know that down-titration of RAAS inhibitors in patients with systolic heart failure is associated with worse outcome and increased mortality and these patients can tolerate S-K up to 5.5 mmol/L [9,11]. A combination of ACE-I and ARB, as in case 2, should be avoided because combined therapy places the patient at special risk for hyperkaliemia without proven benefit [2].

These patients also received beta-blockers (BB) and patient 2 was intoxicated by digoxin. BB and digoxin at toxic levels decrease the activity of the Na^+/K^+-ATPase and increase S-K [7].

Acute episodes of hyperkaliemia are commonly triggered by the introduction of a medical product affecting potassium homeostasis, such as NSAID (nonsteroidal anti-inflammatory drugs) in case 1, also illness or dehydration can be triggers [7,10], like dehydrating diarrhea causing prerenal failure in case 2. NSAIDs have an MRA-effect and can impair renal function and induce severe hyperkaliemia, which is what happened in case 1. The risk of such NSAID side effects is increased in patients with renal disease and in patients treated with other RAAS inhibitors [6,7].

For some weeks before admission, both patients exhibited symptoms consistent with severe hyperkaliemia, in the form of pronounced muscular weakness. Their survival may be due to adaptation and increased tolerance to hyperkaliemia, even though an increased toxicity to hyperkaliemia could be anticipated in patient 1 due to ischemic heart disease and sick sinus syndrome and in patient 2 due to digoxin intoxication and atrial fibrillation [2].

ECG change is not obligate in hyperkaliemia but occurs increasingly as S-K increases [3,5]. Classic ECG-changes are illustrated in Figures 1 and 2 and suggest the presence of hyperkaliemia.

Early rises in the extracellular potassium concentration level lower the resting cardiac membrane potential and increase the cardiac conduction velocity. This gives rise to narrow-based, tall, peaked, and symmetric T-waves and QT-shortening. Increasing S-K results in conduction delay and manifests as progressive prolongation of the P-wave, PR-interval, and QRS-complex [4]. In severe hyperkaliemia, P-waves may disappear, QRS widens corresponding to nonspecific intraventricular block, T-waves broadens, and there may be SA- and/or AV-block, junctional rhythm, and ventricular extrasystoles. As S-K increases further, progressively slowed depolarization is observed.

The QRS-complexes widen and merge with the broad T-waves resulting in sine waves (Figure 1) which are associated with excessive and pre-terminal hyperkaliemia; this is a warning of imminent heart stop in ventricular fibrillation or asystolia [2-4,6].

Survival of hyperkaliemia with a concentration of approximately 10 mmol/L, as in the two cases presented here, strongly indicates the efficacy of what has become the standard treatment of excessive hyperkaliemia [3].

Table 1: Treat severe hyperkaliemia in the following order and the regime can be repeated.

• 10 mL/1 vial of Calcium Chloride 10% (1 g) intravenous (IV) **OR** (equipotent) 30 mL/3 vials of Calcium Gluconate 10% (3 g) IV.
• 50 mL 50% Glucose, and 10 IU rapid-acting Insulin.
• Beta-2-agonist inhalation for example Salbutamol 10 mg to 20 mg (optionally IV).
• Furosemide 40 mg to 80 mg IV, provided there is diuresis.
• Sodium Bicarbonate infusion in patients with severe metabolic acidosis, 100 mL 8.4%.
• Emergency Hemodialysis.

Table 2: The positive reaction to the treatment of hyperkaliemia (Table 1) is documented by decreases in S-K from 9.9 mmol/L to 8.3 mmol/L and then to 5 mmol/L after dialysis, but with temporary rebound effect followed by normalization of S-K, S-creatinine, pH, and S-digoxin.

Time	S-K	S-crea.	pH	S-digoxin
Day 1				
23:12	9.7	337	7.23	
23:28	9.9	368	7.18	4.6
Day 2				
0:39	8.4		7.26	
1:02	8.2		7.27	
1:53	8.3		7.27	
2:29	7.9		7.29	
3:44	6.6		7.37	
4:56	5.7		7.38	
5:27	5.3		7.41	
7:06	5	231		3.1
11:12	4.8		7.36	
13:00	5.6	234		
17:28	5.7			
19:40	5.3			
21:33	5.1			
21:56		207		
23:26	4.7			
Day 3				
1:51	4.7			2.9
4:08	4.6			
6:15	4.9	166		2
6:47	4.9			
10:41	4.9			
Day 4	4.3	122		
Day 5	4.2	123		
Day 6	4.1	109		
Day 7	4	106		
Day 8	4.1	102		
Day 9	4.1	101		

As thresholds for initiation of emergency therapy it is recommended to use S-K >6.5 mmol/L or any elevated level associated with ECG-manifestations of hyperkaliemia [3], circulatory failure, neuromuscular weakness, and/or decreased renal function with severe acidosis [7].

Until urgent, definitive, and essential treatment with dialysis can be performed, the patient should be treated according to Table 1.

Calcium should be administered as early as possible to stabilize the myocardium and protect against arrhythmias, but it does not affect the S-K [7]. Improvement in the ECG should be apparent within two to three minutes of administration of calcium but lasts only 30-60 minutes [4], repeated doses can be given [3,7]. In a patient with both severe hyperkaliemia and digoxin intoxication, as in case 2, calcium should be given slowly and with caution [4,12].

The most effective and expedite way to lower S-K is by treating the patient with Insulin-Glucose combined with a beta-2-agonist, for example Salbutamol, given as inhalations in a nebulizer. Both treatments stimulate the Na^+/K^+-ATPase in the cell membrane which increases the influx of potassium into the cells, thereby temporarily lowering S-K [3,12]. However, initially the beta-2-agonist may increase S-K and for this reason, Insulin-Glucose should be administered before the beta-2-agonist. Insulin also lowers the blood glucose level, whereas the beta-2-agonist increases it. Combination treatment acts synergistically and lowers S-K by 1.2 mmol/L within one hour. The effect of both treatments begins approximately 15-20 minutes after administration and lasts a couple of hours [3,12].

Both patients had severe renal metabolic acidosis (pH < 7.2 and S-hydrogencarbonate <17 mmol/L), which shifts potassium into the extracellular space and thus increases S-K. This should be treated with an infusion of bicarbonate [7,8,12].

Forced diuresis with fluid and a loop diuretic increases the elimination of potassium from the kidneys, depending on the renal function.

The treatments summarized in Table 1 should be repeated regularly until dialysis can be performed. Dialysis is the only efficient way to remove potassium rapidly and it is a

necessary and ultimate treatment of extreme hyperkaliemia [2,6,8,12].

A Resonium enema could be considered, but other treatments must have higher priority, as it takes hours before Resonium has any effect [8]. The content of potassium is high in the colon where Resonium binds potassium leading to increased elimination of potassium [3,7]. Oral administration of Resonium takes even longer (four to six hours) to increase the elimination of potassium [7]. For the same reason the new Patiromer is not indicated in the treatment of acute and excessive hyperkaliemia [8].

The patients responded to the treatment while waiting for the dialysis. Afterwards they recuperated (Table 2) and were discharged in good condition. Although hyperkaliemia is life threatening, it can be treated faster than most other dangerous conditions and emergency treatment may be immediately lifesaving.

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