

Trimethoprim related Hyperkalaemia in a patient with Renal Tubular Acidosis Type 4

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Learning points

- Trimethoprim can cause hyperkalemia, even at normal doses, due to inhibition of potassium excretion.
- Particular care should be taken with trimethoprim in patients with known chronic kidney disease or previous adverse reaction to angiotensin converting enzyme inhibitors.
- Keeping separate case files for medical and psychiatric care can potentially compromise the dissemination of life saving information such as drug allergies and medical alerts.

Abstract

Hyperkalaemia is a common, treatable, medical emergency, often with an iatrogenic cause. This case illustrates the vulnerability of patients with pre-existing renal tubular acidosis type 4 to medications that further inhibit renin-aldosterone action. The case also illustrates the danger of keeping entirely separate case notes between different hospital disciplines.

Keywords

Trimethoprim, hyperkalaemia, renal tubular acidosis type 4

Introduction

Hyperkalaemia is a common medical emergency in medical patients, requiring immediate management to prevent life-threatening cardiac arrhythmias. In many cases the cause is iatrogenic, due to a range of drugs which inhibit potassium excretion.¹ Following treatment to reduce potassium levels in the acute setting, attention needs to be paid to the underlying cause of the hyperkalaemia to re-establish the normal homeostatic mechanisms that maintain a normal plasma potassium level.

In elderly medical patients there are often multiple pre-existing co-morbidities (as well as age related changes in physiology) that predispose to heightened adverse responses to even low doses of common medications. It is important therefore to ensure information of any prior allergies or adverse reactions are readily available to all prescribers for that patient.

The following case illustrates the vulnerability of patients with pre-existing renal tubular acidosis type 4 to medications that further inhibit renin-aldosterone action.

It also demonstrates the pitfalls in keeping entirely separate case notes between different hospital disciplines.

Case History

A 74 year old lady under psychiatric in-patient care was referred to the on-call acute medical team after blood tests had revealed hyperkalaemia (potassium 6.8mmol/l). The psychiatric junior doctor had requested a set of bloods, including urea and electrolytes to monitor response to treatment for a recent urinary tract infection. She had a prior history of stage 2 chronic kidney disease (eGFR of 70), due to diabetic nephropathy, on a background of stable ischaemic heart disease, chronic congestive cardiac failure and iron deficiency anaemia.

The patient had been reluctant to engage fully with either the medical or psychiatric team with regards to any changes in her medication, or give detail on her past medical history. However, it was known that she had been diabetic for quite some years with a diagnosis of ischaemic heart disease of similar duration. She was known to mental health services with a history of previous severe depressive episodes. It was also known that she had been an inpatient three months earlier under the medical team with a non ST elevation myocardial infarct (NSTEMI). The full details of this episode were not known to the psychiatric team.

This current inpatient episode had started when the patient was admitted three weeks previously under the care of the physicians following an overdose of co-codamol 8/500. She had not sustained any persisting organ damage on biochemical and coagulation studies. Potassium level had remained within normal limits throughout that admission. She was subsequently transferred to the elderly adult psychiatry ward for further treatment, having been judged at serious risk of repeated self harm.

The psychiatric team had continued her medications as documented by the original admitting medical team, from whose care they had

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received the patient. These were Omeprazole 40mg od, Ferrous Sulphate 200mg bd, Clopidogrel 75mg od, Diltiazem m/r 120mg od, Simvastatin 40mg nocte, Metformin 500mg tds, Quinine Sulphate 300mg od, Lactulose 10ml bd, Mirtazepine 30mg nocte and Zopiclone 3.75mg nocte.

Physical examination at the time of her second admission revealed no evidence of acute congestive cardiac failure and normal cognition. An ECG showed sinus rhythm, 80bpm, with PR, QT and QRS intervals within normal limits. There was no change in T-wave morphology from previous ECGs.

Following intravenous administration of 15 units short-acting insulin and 50mls of 50% dextrose the serum potassium level fell to 5.7mmol/L. Further biochemistry showed a serum sodium of 132mmol/L, urea of 13.4mmol/L, creatinine of 135µmol/L, with a calculated eGFR of 47. With the exception of the potassium these results were broadly in keeping with recent ones from the medical phase of this admission, at which time it was noted the previously stable eGFR of around 70 had dipped to 50-60. Review of the patient's drug chart confirmed that she had just completed a 5 day course of trimethoprim (200mg BD) for a urinary tract infection (confirmed sensitive proteus species).

The psychiatry team was advised that management should include daily monitoring of urea and electrolytes, keeping a fluid balance chart to ensure good oral intake of fluids and entering an alert on the patient's case notes to state the risk of iatrogenic hyperkalaemia with trimethoprim in this patient.

The patient's serum potassium remained normal over the course of the next week.

The medical case notes, kept separately from the psychiatry notes, revealed more detail on the admission three months prior to this episode. On this occasion the patient had been admitted acutely short of breath due to acute heart failure following a non-ST-elevation myocardial infarct. At this time the patient had been started on an angiotensin converting enzyme inhibitor (ramipril 2.5mg OD) and was subsequently noted to develop hyperkalaemia (serum potassium 6.7mmol/L). Further investigation at that time had demonstrated a hyperchloraemic compensated metabolic acidosis with a normal anion gap (pH 7.34, pCO₂ 3.83kPa, serum chloride 104mmol/L, serum bicarbonate 17mmol/L). Combined with the patient's medical history of diabetes, this allowed a diagnosis of renal tubular acidosis type 4 (hyporeninaemic

hypoaldosteronism), secondary to diabetic nephropathy. The adverse reaction to ACE inhibitors was clearly documented in the medical case notes.

Discussion

Drug induced hyperkalaemia is a frequent problem in medical patients. This is a well recognised phenomenon with initiation of angiotensin converting enzyme inhibitors² and potassium sparing diuretics, for whom monitoring of serum electrolyte levels is common practice after initiation of therapy. Elderly patients and those with pre-existing interstitial nephropathy are at higher risk of this complication as potassium excretion may already be impaired owing to their reduced glomerular filtration rate.³

However, less well recognised is trimethoprim related hyperkalaemia, despite a reasonable body of literature on the mechanism⁴⁻⁶ and clinical risks.⁷ Trimethoprim causes hyperkalaemia by inhibiting potassium excretion. This occurs due to its structural similarity with amiloride. Trimethoprim acts at the sodium channels in the distal nephron. This reduces transepithelial voltage, which impairs potassium excretion at this level.^{4,5} Patients with co-existing renal impairment (such as renal tubular acidosis type 4) are at a more significant risk of developing this complication, even with standard doses of trimethoprim.⁷ An increased awareness regarding the potential risks of trimethoprim prescription, particularly in elderly patients and those with renal impairment, would be of benefit. Previous hyperkalaemia with an angiotensin converting enzyme inhibitor (ACE inhibitor) should raise a clinician's suspicion of the risk of a similar complication with trimethoprim. This may enable the selection of an alternative antibiotic.

NICE guidance for post myocardial infarct states that all patients should be on an ACE inhibitor.⁸ In this case the lack of an ACE inhibitor on the patient's medication list, given her recent NSTEMI should have alerted doctors to the possibility of an underlying previous reaction with this class of drug.

Psychiatric notes are kept separate from medical notes in our hospital. As a result, details of the recent adverse reaction to an angiotensin converting enzyme inhibitor were not readily available to the prescribing physician. Although the significance of this may not have been appreciated by the psychiatry team, it is possible that an alternative antibiotic may have been chosen if this information had been available.

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