National Patient Safety Alert

Medicines & Healthcare products Regulatory Agency

Potential risk of underdosing with calcium gluconate in severe hyperkalaemia

Date of Issue:	27-Jun-23	Reference No:	NatPSA/2023/007/MHRA

This alert is for action by: Acute providers, specifically those providing acute medical care where severe hyperkalaemia is likely to be treated.

This is a safety critical and complex National Patient Safety Alert. Implementation should be coordinated by an executive leader (or equivalent role in organisations without executive boards) supported by Chief Pharmacists, emergency medicine specialists, the clinical leads for cardiology, nephrology, advanced life support, and critical outreach nurse practitioners.

Explanation of identified safety issue:

This alert highlights the Adult Renal Association Clinical Practice Guidelines (2020) recommendation on calcium gluconate use to support organisations to update local policies and guidelines for the treatment of severe hyperkalaemia in adults. The MHRA has also published a Drug Safety Update article with further information.

The MHRA has identified isolated cases where medication errors have occurred due to inadvertent administration of an underdose of calcium gluconate, including one death.

Incident reports from the National Reporting Learning System (NRLS) data suggest that some healthcare professionals may not recognise that a full 30ml dose of calcium gluconate is required to initiate treatment and that repeat doses of calcium salts may be necessary based on clinical monitoring.

The confusion may result from conflicting previous recommendations for giving smaller doses incrementally; and a lack of recognition that doses of calcium salts are not interchangeable.

To achieve the recommended calcium dose of 6.8 mmol: **30ml** of calcium gluconate 10% *or* 10ml calcium chloride 10% must be used. Both calcium gluconate and calcium chloride preparations are available in 10ml vials therefore **3** vials of calcium gluconate are required to reach the dose equivalent to only **1** vial of calcium chloride. The method of administration should be slow intravenous injection in the non-arrested patient. Bolus injection is recommended in cardiac arrest.

A repeat dose may be needed.

Actions required

When: Begin as soon as possible and be completed by 01/12/2023

1. Identify a senior clinician in the organisation to lead the actions in response to this alert.
2. Review local guidance to ensure it aligns with the Adult Renal Association Clinical Practice Guidelines (2020) for the treatment of severe hyperkalaemia – importantly, this includes electronic mobile applications, quick reference guides and supporting materials for clinicians. Where they are in use, hyperkalaemia kits should be aligned with the guidance.
3. Review internal procedures to establish which calcium salt will be the first-line treatment for acute severe hyperkalaemia. Ensure this is standardised across all wards and units so staff are accustomed to using the same product.
4. Put in place a procedure to extend support from critical care outreach teams or advanced life support teams to ensure the time critical treatment for severe hyperkalaemia is implemented.
5. Ensure relevant guidance and resources are embedded in clinical practice by revising local training and audit. Consider using peri arrest/cardiac arrest audits to monitor standardised, safe practice across the board.
6. Consider putting laminated treatment protocols for severe hyperkalaemia in relevant clinical areas.
7. Report calcium gluconate medication errors or near misses via local risk management systems; and medication errors that result in harm on a Yellow Card.

Failure to take the actions required under this National Patient Safety Alert may lead to CQC taking regulatory action

Additional information:

Severe hyperkalaemia (≥ 6.5 mmol/l) is potentially a life-threatening emergency. The risk of associated arrythmias and cardiac arrest increases in proportion to severity of elevated potassium and can be unpredictable. ECG changes may provide evidence of toxicity but may initially not be present.

In 2020, the Adult Renal Association Clinical Practice Guidelines were reviewed, continuing the recommendation from 2014 that 6.8mmol of calcium chloride or calcium gluconate should be used in patients with ECG changes: **30ml** of 10% (w/v) calcium gluconate or **10ml** of 10% (w/v) calcium chloride to stabilise the myocardium and prevent/treat reversible cardiac arrhythmias. [1]

Calcium salts do not reduce serum potassium but are given to stabilise the myocardium and prevent cardiac arrythmia. Measures to lower potassium levels must be instituted immediately. Continue to monitor serum potassium while the underlying cause is being addressed. Involvement from critical care and outreach or advanced life support teams may facilitate more rapid and co-ordinated treatment.

The effect of calcium salts is temporary. A **30ml** IV bolus dose of **calcium gluconate** should be given over 10 minutes [2] (see accompanying Drug Safety Update). Consider repeat doses if adverse ECG changes remain after 5 to 10 minutes. In contrast, a **10ml** IV rapid bolus dose of **calcium chloride** should be given as a single dose. Consider repeat doses if there is no improvement in ECG. ECG monitoring is advised for potassium levels above 6.0mmol/L

Tissue necrosis is a serious adverse event if extravasation occurs during administration of both IV calcium salts. Ensure reliable intravenous access and test with flush prior to administration.

Patient safety incident data

A free text search of potassium, gluconate and chloride was undertaken in NRLS from 01 January 2016 to 31 August 2022. A clinical review of 31 incidents reported as fatal and 25 reported as severe patient harm were identified. Since the reviewed clinical guidelines (August 2020), 6 incidents showed incorrect calcium gluconate administration and monitoring in the context of severe hyperkalaemia and cardiac arrest (5 fatal, 1 unknown outcome). Safety concerns related to underdosing of calcium gluconate administration included lack of repeat dosing where indicated; lack of potassium-lowering treatment and lack of, or inappropriate, ECG monitoring. Healthcare professionals did not seem aware that underdosing was occurring and did not always appreciate that treatment was time critical. One fatal published literature report was identified in which underdosing of calcium gluconate led to subsequent lack of drug effect and contributed to cardiac arrest. No other reported events relating to a 6.8mmol dose have been received.

It is important to note that a causal association between underdosing of calcium gluconate or mismanagement of serum potassium and the patients' outcome cannot be established in reported incidents.

Healthcare professionals are reminded that calcium gluconate is not usually recommended for the treatment of cardiac arrest except where there is concomitant severe hyperkalaemia.[2]

References

1.The Renal Association. Clinical practice guidelines. Treatment of acute hyperkalaemia in adults, J 2020.
2. Resuscitation Council UK. 2021 Resuscitation Guidelines. Special Circumstances Guidelines. Treatment of hyperkalaemia [March 2022] (viewed on 01 November 2022)

Stakeholder engagement

The MHRA has consulted with NHS England and representatives from the Scottish and Welsh Governments, the Department of Health Northern Ireland, and the UK Kidney Association.

To learn more on how alert issuing bodies are working together to issue alerts please go to https://www.england.nhs.uk/patient-safety/national-patient-safety-alerting-committee