

# **Guideline for the perioperative management of people with inherited salt-wasting alkaloses (Gitelman's syndrome and Bartter's syndrome) undergoing non-urgent surgical procedures**

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**The Royal College  
of Anaesthetists**

## **Clinical need for a guideline**

Whilst there are no specific surgical complications of salt-wasting alkaloses (SWA), these patients may require surgical procedures like anyone else. Hypokalaemia and hypomagnesaemia are common in patients with SWA. There are perioperative risks associated with hypokalaemia, which may be potentiated by low magnesium levels. These include arrhythmia, weakness, tetany, ileus, metabolic alkalosis and confusion. ECG changes seen in hypokalaemia included increased P-wave amplitude, prolonged PR interval, apparent QT interval prolongation, reduction in T-wave amplitude, T-wave inversion, ST segment depression and U-waves. However the current perioperative approach in patients with SWA is inconsistent, and patients may equally be denied surgery on the basis of chronic and stable metabolic derangement. The purpose of this guideline is

to reduce this variation and therefore improve practice. The US National Guideline Clearinghouse does not contain existing guidelines on this subject.

## **Methodology of guideline development**

A working group was established, composed of two nephrologists and one anaesthetist. The scope of the guideline was agreed by all parties. Literature searches were run on Cochrane, Medline, Embase, the British Nursing Index, CINAHL, and the Centre for Reviews and Dissemination (University of York) database by Ms Potenza Atiogbe (Epsom & St Helier NHS Trust) between March and May 2012. The search terms included: Gitelman's syndrome and Bartter's with anaesthesia; potassium or magnesium with anaesthesia; and anaesthesia with diuretics. Searches were restricted to Human and English Language papers. The titles and abstracts were screened by each member of the working group independently to determine relevance. Disagreements were resolved by consensus. Relevant full texts were then reviewed by the same observers and graded according to a pre-prepared checklist.

The exploded searches generated a total of 1,886 abstracts, from which 125 were deemed to be relevant, with significant redundancy across the various databases. There were no systematic reviews or meta-analyses of randomised controlled trials (RCT) and no controlled studies of any description, with or without randomisation. Accordingly a narrative review was conducted to inform guideline development, which followed through a series of iterations between the members of the working group. The guideline was submitted for final review by the Renal Association (Professor Fiona Karet, Chair of the Salt-Wasting Alkaloses Rare Disease Working Group) and the Royal College of Anaesthetists.

## **Scope**

### **Groups included in this guideline**

- Adults (aged 18 and over) with existing formal diagnosis of an inherited salt-wasting alkalosis (SWA)

### **Groups not included in this guideline**

- Children with inherited SWA
- Patients with hypokalaemia and/or hypomagnesaemia due to causes other than inherited SWA

### **Remit of the guideline**

The guideline covers:

- The perioperative management of patients undergoing elective or expedited (NCEPOD definition) surgical procedures

The guideline does not cover:

- The management of patients with SWA requiring immediate or urgent surgery (NCEPOD definition)
- The management of non-surgical procedures (eg administration of oral bowel cleansing agents)

The following key areas are addressed:

- Pre-operative assessment of patients
- Minimum acceptable levels of serum potassium and magnesium for elective and expedited surgery to proceed
- Intra-procedural monitoring
- Post-operative monitoring

### **Guideline review date**

February 2018

### **Recommendations for patients with salt-wasting alkaloses undergoing elective or expedited surgery**

1. We suggest that patients with salt-wasting alkaloses have pre-operative assessments for elective or expedited surgery as outlined for the general population in existing national guidance\*, and that:

- all patients (irrespective of ASA grade and grade of surgery) have a pre-operative electrocardiogram
- all patients (irrespective of ASA grade and grade of surgery) have pre-operative testing of serum potassium and magnesium within 24 hours of surgery (rather than solely in a pre-assessment clinic)

2. We suggest that the decision to proceed with elective or expedited surgery based upon pre-operative electrolyte values is an individual case decision based upon:

- the time course of hypokalaemia and hypomagnesaemia (specifically recognising that these abnormalities in patients with SWA are generally chronic)
- the type of surgery and fitness of the patient
- a history of dysrhythmia or the presence of abnormalities on the resting electrocardiogram
- pre-existing cardiovascular risk factors
- concurrent electrolyte abnormalities
- concurrent medications (including digoxin, beta-2 agonists and insulin)

3. We suggest that in an asymptomatic patient in whom there are no other markers of risk that it would generally be reasonable to proceed with elective or expedited surgery with a serum potassium of  $\geq 3.0$  mmol/L (provided serum magnesium is  $> 0.5$  mmol/L, see below). For otherwise uncomplicated patients undergoing minor surgery it may be appropriate to proceed with serum potassium  $\geq 2.8$  mmol/L where there is clear evidence that the abnormality is stable.

4. Where there is evidence of concurrent severe hypomagnesaemia ( $< 0.5$  mmol/L) we suggest that a reasonable safe lower limit of serum potassium for elective or expedited surgery is  $\geq 3.3$  mmol/L.

5. We suggest that patients whose serum potassium or magnesium is below these thresholds are referred back to a physician with expertise in the management of salt-wasting alkaloses for advice on diet and drug treatment, and re-scheduled for surgery when the electrolytes are above the threshold. If it proves impossible to achieve stable serum potassium  $> 3.0$  mmol/L with serum magnesium  $> 0.5$  mmol/L, then the patient should be offered surgery after full discussion of the risks and benefits, with the option of carefully monitored intravenous electrolyte replacement peri-operatively.

6. Recognising the morbidity and mortality associated with the rapid correction of electrolyte abnormalities, we suggest that pre-operative administration of intravenous potassium and magnesium should be avoided for patients undergoing elective or expedited surgery.

7. We recommend that clinical practice guidelines on the need for fasting prior to surgery are followed.

8. We suggest that monitoring during anaesthesia and recovery should be performed as outlined in national guidance\* for the general population, and that:

- facilities should be available for the rapid assessment and correction of electrolyte abnormalities
- intraoperative muscle relaxation should be guided by the use of a peripheral nerve stimulator
- continuous ECG monitoring should be available during recovery
- post-operative high dependency care is available for patients in whom potassium levels are unstable, are vomiting or are at high risk of ileus
- day case surgery may be appropriate for patients with stable potassium levels undergoing low risk procedures

9. We suggest that for major surgical procedures, for example abdominal hysterectomy, endoscopic resection of prostate, lumbar discectomy and thyroidectomy, electrolytes (including potassium and magnesium) are measured immediately after surgery, with the need for further testing dictated by the clinical circumstances.

10. We suggest that the use of invasive arterial monitoring for serial peri-operative blood sampling is considered in the most complex cases.

\*Key national guidance documents

- The NCEPOD classification of intervention (NCEPOD, 2004)
- The use of routine preoperative tests for elective surgery (National Institute of Health and Clinical Excellence, 2003)
- ACC/AHA Guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery (Circulation, 2014)
- ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management (European Heart Journal, 2014)

- Recommendations for standards of monitoring during anaesthesia and recovery 4<sup>th</sup> edition (Association of Anaesthetists of Great Britain and Ireland 2007)
- Perioperative fasting in adults and children: an RCN guideline for the multidisciplinary team (Royal College of Nursing 2005)

## **Narrative summary of supporting evidence**

Gitelman's and Bartter's syndrome are rare inherited disorders whose clinical features arise as a result of impairment of sodium chloride reabsorption in the distal tubule (Gitelman's) or loop of Henle (Bartter's). The prevalence of Bartter's and Gitelman's syndrome has been estimated at 1:40,000 and 1:1,000,000 respectively from the Framingham study. Secondary hyperaldosteronism occurs as a result of renal salt wasting in both conditions resulting in hypokalaemia and metabolic alkalosis. In Gitelman's syndrome hypomagnesaemia also arises as a result of renal magnesium wasting. Hypomagnesaemia is also seen in Bartter syndrome Type III. The tubular defects seen mimic those of long-term thiazide (Gitelman's) or loop (Bartter's) diuretic use. Blood pressure is frequently low or normal (at least until mid-adult life) and renal excretory function is preserved. Treatment of patients with salt-wasting alkaloses involves life-long supplementation with sodium chloride, potassium chloride, and magnesium salts, together with potassium-sparing diuretics and non-steroidal anti-inflammatory drugs.

Hypokalaemia and hypomagnesaemia are known to affect neuromuscular excitability by effects on the action potential. Both abnormalities increase the risk of tachyarrhythmias; the absolute risk, however, is highly dependent on the presence of other risk factors for tachyarrhythmias, such as ischaemic, hypertensive, or valvular heart disease.

QTc prolongation on electrocardiography is evident in up to 40% of patients with Gitelman's syndrome (1) and patients with salt-wasting alkaloses may be at increased risk of ventricular tachycardia and sudden cardiac death (2)(3). However there is a paucity of evidence of any level from which to make recommendations concerning perioperative management of these patients. Evidence specific to Bartter's (4)(5)(6)(7)(8)(9)(10) and Gitelman's (11)(12)(13) syndrome is largely confined to the setting of case reports from the paediatric and adult literature, which describe a range of anaesthetic practice.

There is one case series examining perioperative management in patients with Gitelman's syndrome (14). The records of 42 patients with presumed Gitelman's syndrome from a single centre were retrospectively reviewed; 5 had undergone surgical procedures requiring anaesthesia. Preoperative values for potassium and magnesium ranged from 3.2 - 4.0 mmol/L and 0.49 - 0.66 mmol/L respectively. No acute electrolyte problems or post-operative complications were observed. The authors concluded that a preoperative ECG and electrolytes should be checked before most procedures, with further testing guided by the history, and that, whilst complete correction may not be achievable, near-normal values of potassium and magnesium should be sought.

Additional, albeit indirect, information is available from a small number of studies examining the relationship between hypokalaemia and hypomagnesaemia more generally and perioperative dysrhythmia in patients with varying degrees of cardiovascular co-morbidity. A prospective study of 447 patients undergoing major vascular or cardiac surgery, 93% with known cardiac disease, concluded that there was no relationship between dysrhythmias and serum potassium levels; 9% in this study had serum potassium <3mmol/L (15). A second prospective study of 150 patients suggested that potassium levels as low as 2.6 may be safe in a study population including 23% with cardiac disease (16).

An article reviewing the anaesthetic implications of hypokalaemia emphasised that clinical experience suggested that patients with hypokalaemia tolerated a variety of anaesthetic regimens and surgical interventions without difficulty, but that these experiences had not been collated, and that the literature was biased towards anecdotal reports of patients with severe intraoperative dysrhythmias found in retrospect to be hypokalaemic. The authors concluded that the common practice of cancellation or repletion in asymptomatic patients was not supported by the evidence and that a value of 3mmol/L was a reasonable and conservative value for undertaking elective surgery. They emphasised a risk based approach, taking into consideration: the aetiology and time course of the patient's hypokalaemia; concurrent medications such as digoxin or other antiarrhythmics; underlying cardiac function and risk for myocardial ischemia; ECG evidence of hypokalemia with special attention to increased ventricular dysrhythmias; contemplated surgery; and urgency/emergency of surgery (17). The importance of time course is illustrated by consideration of the basic physiology of excitable membranes. It is the ratio of intracellular : extracellular fluid potassium that is essential for the maintenance of membrane potential (18). In chronic disorders of potassium balance the ratio is well-maintained, but acute

changes result in symptoms through disturbance of the ratio. Emergency potassium repletion carries a risk of life threatening reaction of 1:175 (19).

Dysrhythmias are also associated with hypomagnesaemia. However concurrent hypokalaemia is a consistent cofounder (20) and a review article concluded that there was no evidence that isolated hypomagnesaemia was pro-arrhythmic but that it may exacerbate potassium-mediated dysrhythmias (21).

Specific perioperative issues have been discussed in the context of patients with Bartter's syndrome (8) and Gitelman's syndrome (14), and in patients with hypokalaemia more widely (22). Medications that prolong the QT interval and/or worsen electrolyte abnormalities (including preoperative bowel preparation, beta-2 agonists and insulin) should be avoided where possible. Nasogastric suction and hyperventilation may also exacerbate hypokalaemia. Other factors which may need to be taken into consideration include the potential of hypokalaemia to prolong neuromuscular blockade (23) and of epinephrine used in the administration of regional blocks to cause hypokalaemia (24). Post-operatively, hypokalaemia is a recognised cause of ileus and it should also be remembered that the rate of potassium loss may be increased after surgery (25).

We do not have definitive evidence to suggest exact pre-operative levels of potassium and magnesium that are safe. This review of the literature emphasises the need for careful pre-operative risk stratification and intra- and post-operative monitoring as outlined in existing national guidance (26)(27)(28)(29)(30), using the limited evidence available to tailor these guidelines to the setting of patients with pre-existing metabolic disturbances, in order to inform decisions that must always be taken on a case by case basis.

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## **Declarations of Interest**



The authors do not have any relationships with any organisation with a financial interest in the subject of this guideline, nor any other pecuniary or non-pecuniary conflicts of interest relevant to its preparation.

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