GUIDELINES

Secondary prevention for patients after a myocardial infarction: summary of updated NICE guidance

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Acute management of people who have had a myocardial infarction (MI) has changed dramatically, with more people surviving. More effective treatment, including percutaneous coronary intervention, raises questions about the relevance of current recommendations on secondary prevention. Concerns have arisen about the need for the anti-platelet regimens mandated by coronary stent insertion in people who have an independent need for warfarin. New data are also available about how to increase attendance for cardiac rehabilitation programmes, about existing drug treatments and lifestyle advice, and new antithrombotic agents.

The impact of shorter stays in hospital on the changes in acute management have emphasised the importance of primary care in secondary prevention. General practitioners and nurses are now responsible for most of this activity, specifically the promotion of cardiac rehabilitation programmes and the prescription and monitoring of ongoing drug therapy. This also requires effective communication between hospital and primary care, ensuring that clear management plans are relayed in a timely way.

These considerations have led to a revision of the 2007 guideline on secondary prevention after an MI. This article summarises the most recent recommendations from the National Institute for Health and Care Excellence (NICE).

Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Development Group’s experience and opinion of what constitutes good practice. Evidence levels for the recommendations are in the full version of this article on bmj.com.

Cardiac rehabilitation

Cardiac rehabilitation should be offered to all people who have had an MI and should be provided in different settings (such as in the person’s home) and at different times of the day to ensure that people can attend and complete the programme.

- Offer cardiac rehabilitation programmes designed to motivate people to attend and complete the programme. Explain the benefits of attending (which include reducing the risk of death and of having another MI, and improving quality of life). (New recommendation.)
- Begin cardiac rehabilitation as soon as possible after admission and before discharge from hospital. Invite the person to a cardiac rehabilitation session starting within 10 days of their discharge from hospital. (New recommendation.)

Lifestyle changes after an MI

Lifestyle changes after an MI should focus on smoking cessation, dietary interventions, weight management, moderation of alcohol consumption, and regular physical activity.

- Advise all people who smoke to stop and offer assistance from a smoking cessation service in line with NICE public health guidance on brief interventions and referral for smoking cessation (PH1).
- Advise people to eat a Mediterranean-style diet (more bread, fruit, vegetables, and fish; less meat; and replace butter and cheese with products based on plant oils).
- After an MI, offer all patients who are overweight or obese advice and support to achieve and maintain a healthy weight in line with NICE clinical guideline on obesity (CG43).
- Advise people who drink alcohol to keep weekly consumption within safe limits (no more than 21 units of alcohol per week for men, or 14 units per week for women) and to avoid binge drinking (more than 3 alcoholic drinks in 1-2 hours).
- Advise people to be physically active for 20-30 minutes a day to the point of slight breathlessness. Advise people who are not active to this level to increase their activity in a gradual, stepwise manner, with the aim of increasing their exercise capacity. They should start at a level that is comfortable and increase the duration and intensity of activity as they gain fitness.
- Do not recommend routinely eating oily fish for the sole purpose of preventing another MI. If people after MI choose to consume oily fish, healthcare professionals should be aware that there is no evidence of harm, and fish may form part of a Mediterranean-style diet. (New recommendation.)
- Do not offer or advise people to use the following to prevent another MI:
  - Omega 3 fatty acid capsules
  - Omega 3 fatty acid supplemented foods.
  - If people choose to take omega 3 fatty acids (as capsules or supplemented foods), healthcare professionals should be aware that there is no evidence of harm.
    - (New recommendation.)

Drug therapy

Box 1 summarises the drug treatment recommended to reduce the risk of another MI, with detail in the following text. For details on contraindications, please refer to the British National Formulary.

Angiotensin converting enzyme (ACE) inhibitors

- Offer people who present acutely an ACE inhibitor and continue it indefinitely.
Box 1 | Drug therapy for people who have had an MI
• Angiotensin converting enzyme (ACE) inhibitor
• Dual antiplatelet therapy (low dose aspirin plus a second antiplatelet agent)
• β blocker
• Statin

Refer to relevant NICE guidance on use of prasugrel for treating acute coronary syndromes (technology appraisal 182), on the acute management of MI with ST segment elevation and non-ST segment elevation (clinical guidelines 167 and 94), and on the use of statins (clinical guideline 67, to be updated in 2014).9

• Titrate the dose upwards at short intervals in hospital (such as every 12-24 hours) and ensure complete titration within four to six weeks after discharge. (Updated recommendation.)
• Offer people after an MI who are intolerant to ACE inhibitors an angiotensin receptor blocker instead of an ACE inhibitor. (New recommendation.)
• For patients who have had an acute MI and who have symptoms or signs of heart failure and left ventricular systolic dysfunction, start treatment with an aldosterone antagonist licensed for post-MI treatment within 3-14 days of the MI, preferably after starting ACE inhibitor therapy.

Box 2 includes recommendations on monitoring for people receiving ACE inhibitors and aldosterone antagonists.

Antiplaetelet therapy
• Offer low dose aspirin to all people after an MI and continue it indefinitely. (Updated recommendation.)
• Where aspirin is contraindicated or not tolerated (for example, because of hypersensitivity or a history of dyspepsia):
  – For people with aspirin hypersensitivity, consider clopidogrel monotherapy as an alternative
  – For people with a history of dyspepsia, consider treatment of their dyspepsia in line with NICE clinical guideline on dyspepsia (CG17, currently being updated)10
  – For people with a history of aspirin induced ulcer bleeding whose ulcers have healed and who are negative for Helicobacter pylori, consider treatment in line with NICE guideline on dyspepsia (CG17)10

• Offer clopidogrel in combination with aspirin as a treatment option for up to 12 months to people who have had
  – ST segment elevation MI (characterised by ST elevation or new left bundle branch block on electrocardiogram) and received a bare metal or drug eluting stent
  – Non-ST segment elevation MI (characterised by an absence of persistent ST elevation on electrocardiogram) regardless of treatment. (New recommendation.)

• Ticagrelor in combination with low dose aspirin for up to 12 months is recommended as another treatment option to adults with acute coronary syndromes:
  – Those with ST segment elevation MI whom cardiologists intend to treat with primary percutaneous coronary intervention
  – Those with Non-ST segment elevation MI. (New recommendation.)

• Offer clopidogrel in combination with low dose aspirin for at least one month and consider continuing for up to 12 months for people who have had an ST segment elevation MI for which they received medical management, with or without reperfusion treatment using a fibrinolytic agent. (New recommendation.)

• Offer clopidogrel instead of aspirin to people who have had an MI more than 12 months ago if they also have other clinical vascular disease or are aspirin intolerant, in line with NICE technology appraisal of clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events (TA210). (Updated recommendation.)

The figure outlines antiplaetelet treatment recommendations for people who otherwise need anticoagulation.

β blockers
• Offer a β blocker as soon as possible after an MI, when the person is haemodynamically stable. (New recommendation.)
• Make arrangements (for example, in the discharge summary) to recommend that titration of β blockers occurs up to the maximum tolerated or target dose. (New recommendation.)
• Continue a β blocker for at least 12 months after an MI in people without left ventricular systolic dysfunction or heart failure. (New recommendation.)
• Continue a β blocker indefinitely in people with left ventricular systolic dysfunction. (New recommendation.)

Communication of diagnosis and advice
• Offer a copy of the discharge summary for all people who have had an MI.
• Ensure that the following are part of every discharge summary:
  – Confirmation of the diagnosis of acute MI
  – Results of investigations
  – Incomplete drug titrations
  – Future management plans
  – Advice on secondary prevention. (Updated recommendation.)

Box 2 | Drug monitoring for people who have had an MI

ACE inhibitors
• Monitor renal function (serum creatinine concentration), serum electrolytes, and blood pressure before starting an ACE inhibitor
• Monitor thereafter until treated with a stable dose, and then at least annually
• Consider more frequent monitoring in people at risk of deteriorating renal function, of developing hyperkalaemia, or during an intercurrent illness, particularly when associated with a risk of dehydration

Aldosterone antagonists
• Check renal function and serum electrolytes
• Consider seeking specialist advice if concerned about an increased risk of developing serious hyperkalaemia (such as patients with reduced renal function or if baseline serum potassium is >5 mmol/L)
• Routinely measure blood biochemistry after 48 hours, at 1 and 4 weeks, and at 3 months, and 3 monthly thereafter; and 1 week after a titration upwards in the dose
Antiplatelet therapy in people who have had a myocardial infarction (non-ST segment elevation or ST segment elevation) and who have an additional indication for anticoagulation (for example, atrial fibrillation, pulmonary embolism)

Assess for bleeding risk, thromboembolic risk, and cardiovascular risk

Taking novel oral anticoagulant on admission?

Yes

Consider discontinuing and offering warfarin

No

Type of acute management

Acute management with medical management, balloon angioplasty, or coronary artery bypass surgery

Acute treatment with percutaneous coronary intervention with bare metal or drug eluting stents

No

Aspirin intolerant?

Yes

Offer clopidogrel and warfarin

No

Continue anticoagulation and aspirin

Continue anticoagulation and clopidogrel

After 12 months, continue anticoagulation and consider need for ongoing antiplatelet therapy, taking into account need for anticoagulation, thrombotic risk, bleeding risk, risk of a further coronary event, and patient wishes

RATIONAL TESTING

Investigating hypokalaemia

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A 22 year old woman had a blood test to investigate lethargy at her general practice surgery and was found to have an isolated low serum potassium (2.6 mmol/L; 1 mmol/L–1.5 mmol/L). Her blood pressure was 110/70 mm Hg, and physical examination showed no abnormalities. She was taking no regular drugs and denied taking liquorice or laxatives. She had no recent history of vomiting or diarrhoea.

What is the next investigation? Background

Hypokalaemia is defined as a serum potassium below 3.5 mmol/L and is commonly graded as mild (3.1–3.5 mmol/L), moderate (2.5–3.0 mmol/L), and severe (<2.5 mmol/L). Hypokalaemia is a common finding in the general population; a community based cohort study of 5200 adults over 55 years in the Netherlands showed a 3% prevalence of mild hypokalaemia. It is much more common in hospital populations, with one episode of severe hypokalaemia per week in an observational study at a UK secondary care hospital with a catchment population of 150 000.

Learning points

The cause of hypokalaemia is usually obvious from the history and is most often diuretic drugs or gastrointestinal loss. Severe hypokalaemia (2.5 mmol/L) is associated with life threatening arrhythmias and should be treated in an acute facility with electrocardiographic monitoring. If hypokalaemia is moderate or severe, its cause unclear, consider checking serum and urine electrolytes, renal function, and acid base balance. Refer patients with no obvious explanation for their hypokalaemia for endoclinic or renal assessment.

Overcoming barriers

Implementation of these recommendations will be challenging throughout the healthcare system. Cardiac rehabilitation services need to ensure that people who have had an MI are offered their first cardiac rehabilitation session within 10 days of hospital discharge, and make arrangements to offer further appointments to non-attenders. Hospital services need to review drug policies—particularly around antiplatelet agents, prescribing for people with an independent indication for anticoagulation, and drug titration. Clear and timely communication of management plans, optimising use of discharge summaries, is critical. Primary care teams are largely responsible for the secondary prevention of MI. General practices need to use their in-house systems to identify those who have had a recent MI based on hospital discharge letters and to follow up these patients at an early stage, reviewing management plans, attendance at cardiac rehabilitation, and drug prescription, and providing appropriate lifestyle advice.
About 98% of the body’s potassium is intracellular, and the intracellular-extracellular potassium gradient is crucial to maintaining resting membrane potential and normal nerve and muscle function. Small decreases in extracellular potassium can have serious effects on the heart and skeletal muscles. Mild hypokalaemia is often asymptomatic and picked up on routine blood tests, but severe hypokalaemia is associated with life threatening arrhythmias and sudden cardiac death. In a double blind randomised controlled trial, hypertensive men treated with thiazide diuretics who developed a serum potassium of 3 mmol/L or less had a twofold increase in ventricular arrhythmias compared with those with normal serum potassium.

Is the patient safe?

Because severe hypokalaemia can cause fatal arrhythmias, the first question to answer is whether the patient is in immediate danger (figure). If serum potassium is severely low (<2.5 mmol/L), or if there are symptoms of severe hypokalaemia (such as muscle weakness, syncope, or palpitations), evaluate and treat the patient urgently in an acute facility with cardiac monitoring. Initial assessment of moderate or severe hypokalaemia should include electrocardiography, which may show small T waves, ST depression, prominent U waves, or a prolonged QT interval. Patients with rapid onset of hypokalaemia, concomitant risk factors (especially digoxin treatment, left ventricular hypertrophy, or heart failure), and electrocardiographic changes are at increased risk of serious arrhythmias. The next step is to take a detailed history and examination of the patient. The main laboratory investigations are assessment of serum and urine electrolytes and acid-base balance.

### Algorithm for investigation and management of hypokalaemia

- **Pathway**
  - Life threatening?
    - Potassium <2.5 mmol/L and/or Electrocardiographic changes (U wave, small T, ST depression, arrhythmia) and/or Symptoms (palpitations, syncope, muscle weakness)
    - Risk factors: rapid onset, digoxin treatment, ischaemic heart disease, heart failure, left ventricular hypertrophy
    - Yes
    - Exclude common causes: Diarrhoea/vomiting Diuretics, chronic laxative misuse, liquorice Excess alcohol/nutritional deficiency Insulin treatment for DKA
    - Basic investigations (if hypokalaemia is moderate or severe or its cause unclear): Electrocardiography Renal function and serum electrolytes, including bicarbonate and magnesium Urine electrolytes
    - Cardiac monitor and consider intravenous potassium replacement
    - Urgent inpatient referral
    - Specialist referral (endocrine/renal)
  - No
    - Cause determined
    - Specialist referral (endocrine/renal)
    - Less common causes: Hyperaldosteronism (primary or secondary) Glucocorticoid excess Renal tubular disorders (RTA, Bartter’s syndrome, Gitelman’s syndrome, Liddle’s syndrome) Hypokalaemic periodic paralysis Thyrotoxic periodic paralysis Special investigations: Aldosterone to renin ratio Assessment of glucocorticoid excess Thyroid function tests
    - +/- oral potassium replacement

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**History**

The history often helps clarify the likely cause of hypokalaemia. Gastrointestinal symptoms and a history of diuretic treatment are important because a retrospective observational study found that most cases of hypokalaemia are associated with vomiting or diarrhoea (51%) or diuretics (47%). Reduced oral intake alone rarely causes hypokalaemia in healthy people but is a contributing factor in more than a third of inpatients with severe hypokalaemia. Also ask about a history of excessive alcohol intake, chronic laxative misuse, or liquorice ingestion.

Any process that stimulates uptake of potassium from the extracellular fluid into cells can cause hypokalaemia. This is common after intravenous insulin for treatment of hyperglycaemia (in particular, diabetic ketoacidosis), but stimulation of sympathetic β2 receptors (for example, with high dose salbutamol) and verapamil overdose can have a similar effect. Uptake of potassium by rapidly dividing cells—for example, after vitamin B12 or folate replacement in megaloblastic anaemia—can also cause hypokalaemia. In patients with a history of muscle weakness (typically after strenuous exercise or a large carbohydrate meal) and severe hypokalaemia, consider the possibility of hypokalaemic periodic paralysis or thyrotoxic periodic paralysis (if symptoms of thyrotoxicosis are also present, particularly in Asian men).

**Physical examination**

Look for flaccid muscle weakness and signs of arrhythmias. Check blood pressure because hypertension in association with hypokalaemia may suggest primary hyperaldosteronism or Cushing’s syndrome. In this last scenario, clinical features of steroid excess—such as central obesity, bruises, and proximal muscle weakness or wasting—may be evident. Signs of dehydration, hypotension, and Kussmaul breathing in a patient with diabetes are suggestive of diabetic ketoacidosis.

**Laboratory investigations**

In mild hypokalaemia with an obvious cause, laboratory investigations will be limited to monitoring serum potassium concentrations. However, if hypokalaemia is moderate or severe, or the cause of hypokalaemia is unclear, initial basic laboratory investigations should include sodium, potassium, creatinine, urea, magnesium, glucose, and bicarbonate (figure). Spurious hypokalaemia may occur due to in vitro redistribution—for example, potassium uptake by large numbers of abnormal white cells in leukaemia when the sample is left at room temperature. If this is suspected, send a fresh blood sample to the laboratory for reanalysis of potassium, making sure that the sample arrives rapidly after venepuncture.

**Assessment of acid-base balance**
Investigating presents in childhood

Key feature

- High ketones; potassium drops after intravenous
- High blood pressure

When to order an

- Abnormal liver function

Investigating

- Ж (chest pain)
- Troponin in patients with Ж

When to order an antinuclear antibody test (BM 2013;347:f5060)

- High sensitivity cardiac troponin in patients with chest pain (BM 2013;347:f4222)
- Investigating microcytic anaemia (BM 2013;346:f3154)
- Investigating hypocalcaemia (BM 2013;346:f2213)

Acid-base disturbance and hypokalaemia

<table>
<thead>
<tr>
<th>Type of disturbance</th>
<th>Key feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea, laxative misuse, and other lower gastrointestinal loss</td>
<td>Normal serum chloride</td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td>High ketones; potassium drops after intravenous insulin is administered</td>
</tr>
<tr>
<td>Renal tubular acidosis</td>
<td>Associated with autoimmune disease (type 1) and Fanconi’s syndrome (type 2)</td>
</tr>
</tbody>
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Hypokalaemic acidosis

| Vomiting and other upper gastrointestinal loss | Low serum chloride |
| Mineralocorticoid excess (such as primary hyperaldosteronism) | High blood pressure |
| Hereditary renal channelopathies:              |                   |
| Bartter’s syndrome                             | Presents in childhood        |
| Gitelman’s syndrome                            | Often asymptomatic, presents in adulthood                                 |
| Liddle’s syndrome                              | High blood pressure, low renin and aldosterone                            |
| Diuretic use                                   | Drug history                 |

Measurement of serum bicarbonate can help assess acid-base balance. Acutely, bicarbonate is low in metabolic acidosis and high in metabolic alkalosis, but interpretation can be difficult in chronic compensated acid-base disorders. In this last situation, analysis of arterial blood gases allows complete assessment of respiratory and metabolic components of acid-base disturbance.9

The table summarises common acid-base disorders associated with hypokalaemia. Diarrhoea and other low gastrointestinal disorders (including laxative misuse) can cause hypokalaemia and metabolic acidosis due to direct potassium and bicarbonate loss. Diabetic ketoacidosis is also associated with metabolic alkalosis, whereas renal potassium wasting (see below) with acidosis points towards renal tubular acidosis as a possible cause.

Conversely, excessive vomiting leads to metabolic alkalosis and hypokalaemia (from potassium loss in vomit, aldosterone dependent sodium reabsorption in response to hypovolaemia, and reabsorption of hydrogen ions in response to alkalosis at the expense of potassium loss in the distal nephron). In addition, low serum chloride is common after chronic vomiting, owing to direct loss of chloride. Hypokalaemia associated with alkalosis also occurs in patients taking diuretics; patients with mineralocorticoid excess; and disorders such as Bartter’s syndrome, Gitelman’s syndrome, and Liddle’s syndrome, which are caused by mutations in the diuretic sensitive ion transporters.

Assessment of renal potassium loss

Assessment of urine potassium can help to determine whether hypokalaemia is due to renal potassium loss, when the cause is not obvious. A spot urine potassium, 24 hour urine potassium, creatinine ratio (KCR) can all be used to assess renal potassium loss. One small study showed that a urine KCR of 2.5 mmol/mmol or more was accurate at discriminating hypokalaemia due to renal potassium wasting from a non-renal cause.9 Urine KCR performs better than a random urine potassium concentration alone, without the need for 24 hour collections of urine, and is the most practical way to assess renal potassium loss.

Diuretics are the most common cause of hypokalaemia due to renal loss of potassium. Rarer causes that should be considered when the common causes are excluded include renal diseases such as renal tubular acidosis (often associated with autoimmune diseases such as Sjögren’s syndrome) or hereditary renal tubular disorders (such as Bartter’s or Gitelman’s syndrome).

Assessment of magnesium

An assessment of serum magnesium is important because hypokalaemia and hypomagnesaemia often coexist, and treatment of hypokalaemia is unlikely to be successful without reversal of hypomagnesaemia.10 Check magnesium if the cause of hypokalaemia is not obvious or hypokalaemia is moderate to severe.

When to refer?

Severe hypokalaemia warrants referral to an acute hospital. Refer patients with ongoing hypokalaemia with no explanation for specialist endocrine or renal assessment.

Other specialised tests

After referral, specialised tests are sometimes needed to determine the cause of hypokalaemia. The assessment of plasma aldosterone to renin ratio is considered the most reliable tool for investigating primary hyperaldosteronism, with a retrospective study showing a sensitivity and specificity of 97% and 94%, respectively.11 This ratio is raised in primary hyperaldosteronism and should be assessed in patients presenting with hypertension and unexplained hypokalaemia.

Patients with hypokalaemia and clinical features of steroid excess should undergo screening tests (such as 24 hour urinary cortisol, overnight dexamethasone suppression test, or midnight salivary cortisol) for Cushing’s syndrome.12 Check thyroid function tests (serum thyroid stimulating hormone and free thyroxine) if thyrotoxic periodic paralysis is suspected.

Outcome

The patient was referred to a renal clinic for assessment and was found to have high serum bicarbonate (34 mmol/L; reference range 22-30). Hypokalaemia and metabolic alkalosis fitted with either upper gastrointestinal potassium loss or renal potassium loss due to diuretics, Bartter’s syndrome, or Gitelman’s syndrome.

A normal blood pressure made mineralocorticoid excess an unlikely cause. A urinary KCR of less than 2.5 mmol/mmol suggested non-renal potassium loss. Serum chloride was low at 84 mmol/L (reference range 95-108), which fitted with upper gastrointestinal fluid loss. On closer questioning, with the knowledge of these results, the patient confessed to recurrent self induced vomiting to help with weight loss.

Thanks to James Forrer and Hannah Oram (general practitioners), Junaid Zaman (cardiologist), and Rhian Clissold (renal physician) for their helpful comments on the manuscript.

Contributors: RAO wrote the first draft of the manuscript; all authors revised the manuscript and approved the final version. BV is guarantor.

Competing interests: We have read and understood the BMJ Group policy on declaration of interests and declare the following interests: None.

Provenance and peer review: Commissioned; externally peer reviewed.

Patient consent not required (patient anonymised, dead, or hypothetical).

References are in the version on bmj.com.