Maintaining calcium balance: physiology and implications

**AUTHOR** Sharon L. Edwards, MSc, PGCEA, DipN, is senior lecturer, department of nursing and paramedic science, University of Hertfordshire.


This article provides an overview of the physiology of calcium balance and the associated implications for practice. Understanding the physiological principles is vital to ensure patients’ levels of this essential electrolyte are maintained.

Calcium is the most abundant positively charged ion (cation) in the body and is a constituent of the principal mineral of the skeleton. It has a role in cardiac action potentials and pacemaker activity, and the contraction of cardiac, skeletal and smooth muscle, with implications for myocardial infarction and drug therapies.

In addition, calcium plays an important role in blood clotting and cellular injury and death. Calcium levels are maintained by the kidneys.

**Calcium homeostasis**

Ninety-nine per cent of an adult’s 1,200–1,400g of calcium is in the skeleton and teeth. Less than 1.5g is in the blood, where levels are maintained by hormones within the very narrow range of 9–11mg/100ml.

Calcium requirements are especially high during times of rapid growth in infancy and adolescence, and during pregnancy and lactation. From birth until 10 years, the daily requirement of calcium is 400–800mg, and from 11 to 24 years it is 1,200–1,500mg (Curhan et al, 1993).

In order to maintain the essential regulatory functions mentioned above, the reservoir of calcium in bone is mobilised in deficiency to ensure plasma and intracellular concentrations are kept within a strictly controlled range.

Approximately 98 per cent of the calcium filtered by the kidneys is reabsorbed into the blood (Marieb, 2004).

Phosphate is the primary negatively charged ion (anion) in the intracellular fluid. Adults who are getting enough calcium in their diet are usually also getting the daily dietary requirement of phosphate (800–1,300mg) because both are present in many of the same foods and they generally work in unison.

**Hormonal control**

Serum calcium rarely deviates from its normal range and is regulated primarily by the interaction of two hormones: parathyroid hormone (PTH) from the parathyroid glands and calcitonin from specialised cells in the thyroid glands (Marieb, 2004).

PTH is released when blood calcium levels decline. It promotes an increase in levels by influencing bones, the small intestine and kidneys. When levels in extracellular fluid or plasma are within normal limits or are high, PTH secretion is inhibited. This initiates the uptake of calcium by bone. Increased amounts of calcium are lost in faeces and urine, and more phosphate is retained.

Calcitonin is an antagonist of PTH. It is secreted from the thyroid gland when blood calcium levels rise. It inhibits bone reabsorption and encourages calcium salt deposits in the bone matrix, reducing blood calcium levels. As levels fall, calcitonin release declines (Guyton, 2000).

**Osteoporosis**

Osteoporosis generally occurs after menopause in women and is caused by a disturbance in calcium metabolism. The use of oestrogen or hormone replacement therapy (HRT) is no longer recommended as the first choice of therapy for preventing osteoporosis (MHRA, 2003).

People with higher peak bone mass are less at risk of osteoporosis, as they can tolerate more bone loss before it has serious effects. Therefore, adequate calcium and vitamin D nutrition throughout adolescence and young adulthood is likely to provide protection in old age (Kohrt et al, 1997).

**Learning objectives**

Each week *Nursing Times* publishes a guided learning article with reflection points to help you with your CPD. After reading the article you should be able to:

- Understand the process of calcium homeostasis;
- Be familiar with the functions of calcium;
- Know the role of parathyroid hormone in calcium levels;
- Understand the problems associated with calcium imbalance.

**REFERENCES**


The absorption of calcium

Dietary calcium is absorbed by an active process in the mucosal cells of the small intestine. Some absorption is passive. Active absorption depends on vitamin D (Marieb, 2004).

The active metabolite of vitamin D, calcitrol, induces synthesis of a calcium-binding protein that permits mucosal cells to accumulate calcium from the intestinal lumen. In vitamin D deficiency absorption is seriously impaired (McCance and Huether, 1997). Most intracellular calcium is in complex and sequestered form in the cell membrane. The free intracellular ionised calcium level depends on energy-requiring processes, which exclude calcium from the cell or sequester it in cell organelles.

Only 0.03 per cent of total body calcium is in plasma, where it is found in three different forms:

- 47 per cent as ionised or free calcium;
- 40 per cent is bound to albumin;
- 13 per cent as complex calcium.

Effects of changes in absorption

Too much calcium (hypercalcaemia) leads to cardiac failure. It is defined as a total serum calcium above 3mmol/L or a free calcium level above 5.5mmol/L. The condition is most often related to malignant tumours and prolonged immobility. Too little calcium (hypocalcaemia) leads to tetany which, if severe, can result in fatal muscular convulsions (Galbraith et al, 1999). It is usually associated with inadequate dietary intake of calcium or vitamin D. Other conditions related to hypo and hypercalcaemia are listed in Table 1.

Acidosis (metabolic and respiratory) weakens the bond between albumin and calcium (Holmes, 1993). This means there is more free calcium leading to hypercalcaemia and all the potential problems that go with this (Table 2).

Alkalosis causes increased binding of calcium by proteins, a decrease in the ionised fraction and a strengthening of the bond between albumin and calcium (Holmes, 1993). It leads to hypocalcaemia and its associated problems (Table 2).

The functions of calcium

Calcium is needed for many metabolic processes:

- The structure of teeth and bones;
- Muscle contractions (including the heart);
- Blood coagulation/clotting;
- Transmission of neural impulses;
- The structure of teeth and bones;
- Muscle contractions (including the heart);
- Blood coagulation/clotting;
- Transmission of neural impulses;

Table 1. Causes of Hypocalcaemia and Hypercalcaemia

<table>
<thead>
<tr>
<th>Hypocalcaemia</th>
<th>Hypercalcaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditions that interfere with the absorption of calcium from the gut include:</td>
<td>Conditions that can increase bone reabsorption and raise serum calcium include:</td>
</tr>
<tr>
<td>- Pancreatitis;</td>
<td>- Adrenal insufficiency;</td>
</tr>
<tr>
<td>- Respiratory alkalosis due to hyperventilation – calcium binds to bicarbonate, meaning less is available for use;</td>
<td>- Hyperparathyroidism – excessive PTH is secreted by a parathyroid adenoma;</td>
</tr>
<tr>
<td>- Renal failure;</td>
<td>- Hyperparathyroidism – lack of parathyroid hormone leads to a drop in calcium levels;</td>
</tr>
<tr>
<td>- Increased excretion in response to stress and increased protein intake;</td>
<td>- Low magnesium levels inhibit parathyroid function;</td>
</tr>
<tr>
<td>- Diarrhoea;</td>
<td>- A high level of phosphate (hypophosphataemia). Phosphate binds to calcium ions, reducing their availability.</td>
</tr>
<tr>
<td>- Alkalosis (hyperventilation);</td>
<td>- Adrenal insufficiency;</td>
</tr>
<tr>
<td>- Overuse of loop diuretics because of excessive calcium loss;</td>
<td>- Respiratory alkalosis due to hyperventilation – calcium binds to bicarbonate, meaning less is available for use;</td>
</tr>
<tr>
<td>- In patients with burns calcium can become trapped in burnt tissue;</td>
<td>- Renal dysfunction (decreased excretion);</td>
</tr>
<tr>
<td>- Blood transfusion of banked blood;</td>
<td>- Thiazide diuretics;</td>
</tr>
<tr>
<td>- Hypoparathyroidism – lack of parathyroid hormone leads to a drop in calcium levels;</td>
<td>- Vitamin D intoxication seen in a number of granulomatous conditions. Steroids will turn off the increased production of vitamin D;</td>
</tr>
<tr>
<td>- Low magnesium levels inhibit parathyroid function;</td>
<td>- Tuberculosis;</td>
</tr>
<tr>
<td>- A high level of phosphate (hypophosphataemia). Phosphate binds to calcium ions, reducing their availability.</td>
<td>- Cushing’s disease accompanied by osteoporosis;</td>
</tr>
</tbody>
</table>

Table 2. Causes of Hypocalcaemia and Hypercalcaemia

<table>
<thead>
<tr>
<th>Hypocalcaemia</th>
<th>Hypercalcaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditions that interfere with the absorption of calcium from the gut include:</td>
<td>Conditions that can increase bone reabsorption and raise serum calcium include:</td>
</tr>
<tr>
<td>- Pancreatitis;</td>
<td>- Adrenal insufficiency;</td>
</tr>
<tr>
<td>- Respiratory alkalosis due to hyperventilation – calcium binds to bicarbonate, meaning less is available for use;</td>
<td>- Hyperparathyroidism – excessive PTH is secreted by a parathyroid adenoma;</td>
</tr>
<tr>
<td>- Renal failure;</td>
<td>- Hyperparathyroidism – lack of parathyroid hormone leads to a drop in calcium levels;</td>
</tr>
<tr>
<td>- Increased excretion in response to stress and increased protein intake;</td>
<td>- Low magnesium levels inhibit parathyroid function;</td>
</tr>
<tr>
<td>- Diarrhoea;</td>
<td>- A high level of phosphate (hypophosphataemia). Phosphate binds to calcium ions, reducing their availability.</td>
</tr>
<tr>
<td>- Alkalosis (hyperventilation);</td>
<td>- Adrenal insufficiency;</td>
</tr>
<tr>
<td>- Overuse of loop diuretics because of excessive calcium loss;</td>
<td>- Respiratory alkalosis due to hyperventilation – calcium binds to bicarbonate, meaning less is available for use;</td>
</tr>
<tr>
<td>- In patients with burns calcium can become trapped in burnt tissue;</td>
<td>- Renal dysfunction (decreased excretion);</td>
</tr>
<tr>
<td>- Blood transfusion of banked blood;</td>
<td>- Thiazide diuretics;</td>
</tr>
<tr>
<td>- Hypoparathyroidism – lack of parathyroid hormone leads to a drop in calcium levels;</td>
<td>- Vitamin D intoxication seen in a number of granulomatous conditions. Steroids will turn off the increased production of vitamin D;</td>
</tr>
<tr>
<td>- Low magnesium levels inhibit parathyroid function;</td>
<td>- Tuberculosis;</td>
</tr>
<tr>
<td>- A high level of phosphate (hypophosphataemia). Phosphate binds to calcium ions, reducing their availability.</td>
<td>- Cushing’s disease accompanied by osteoporosis;</td>
</tr>
</tbody>
</table>

References


References


Guided Reflection

Use the following points to write a reflection for your PREP portfolio:

- Outline where you work and why this article is relevant to your practice;
- Highlight something new that this article has taught you about calcium balance;
- Outline the key points this article has taught you about the different functions that calcium has in the body;
- Discuss how you could apply what you have learnt to one of your patients;
- Explain how you intend to follow up what you have learnt in your future practice.

Cell membrane stability and permeability

Although most of the body’s calcium is in bone, its most important practical functions are maintaining muscle contractility and forming clots. It is also implicated in cellular death from hypoxia.

Muscle cell contraction

When a muscle contracts its constituent fibres shorten. Calcium is required in this process. The nerve impulse leading to contraction causes an increase in calcium ion concentration in muscle cells. When a muscle is at rest, intracellular calcium is kept low by the continuous action of the calcium pump that moves calcium back into the extracellular fluid (Marieb, 2004).

Calcium is also needed to trigger cardiac contraction. Ionic calcium enters cardiac cells from the extracellular fluid space during cardiac contraction and, once inside, stimulates the release of larger amounts of calcium from intracellular stores. Ionic calcium is prevented from entering non-stimulated cardiac fibres. But during electrical stimulation of the fibres, the voltage across their cell membrane changes and opens calcium channels, allowing calcium entry into the cells (Guyton, 2000).

These channels are called slow calcium channels because channel opening is delayed. The calcium surges across the membrane and prolongs depolarisation briefly, producing a plateau in the action potential tracing. During the return of cardiac cells to their resting state (re-polarisation), calcium ions go back to their original position within the cell and in extracellular fluid.

Calcium is also needed for the action potential of cardiac cells to enable them to contract, and it is calcium that provides the signal via troponin (cardiac enzyme) binding (Edwards, 2002). Therefore, calcium can be used to diagnose a myocardial infarction, and some drug therapies manipulate it to enhance cardiac functioning. The level of troponin can be used to diagnose the severity of a myocardial infarction.

Calcium channel blockers

These drugs interfere with calcium transport across the plasma membrane, inhibiting muscle contraction (Galbraith et al, 1999). They inhibit the inward movement of calcium ions into vascular and cardiac muscle that occurs during depolarisation.

Calcium channel blockers are most often used to enhance blood flow through the heart. This is achieved by relaxing smooth muscle in the walls of the cardiac blood vessels, promoting dilation and reducing the force of contraction of the heart.

Calcium channel blockers have great therapeutic value as they significantly decrease the workload of the heart and vascular resistance (Galbraith et al, 1999). The ultimate outcome is a decrease in myocardial oxygen demand and an increase in blood flow to the heart. Their use is indicated in angina pectoris and hypertension.

A group of calcium channel blockers are recognised as class IV antiarrhythmic agents (Galbraith et al, 1999). Their main effect is to suppress the activity of the sinoatrial and atrioventricular nodes. As a result, impulse generation and conduction from atria to ventricles is slowed.

These drugs depress phase 4 depolarisation of the atrioventricular node, which is dependent on calcium influx. They also increase the refractory period of the heart. This class of drugs can be used for atrial, supraventricular and ventricular arrhythmias (Galbraith et al, 1999).

Blood clotting

Blood usually flows smoothly past the intact lining of blood vessels. But if the walls are breached, a series of reactions is set in motion to accomplish haemostasis (Guyton, 2000). Blood clotting involves a number of processes and factors. Factor IV involves calcium ions and is needed for essentially all stages of coagulation (Marieb, 2004).

Cell death and calcium

Calcium is necessary for maintaining the action potential of muscle and consequent contraction. Calcium rushes into the cell during depolarisation (muscle contraction), and is quickly removed by the continuous activity of the calcium transport pump. The accumulation of calcium in a cell is one of the effects of hypoxia. If calcium is allowed to accumulate in a cell due to a failure of the calcium pump, this accumulation leads to cell death. This occurs in conditions such as pressure ulcers, MI, compartment syndrome, deep vein thrombosis, pulmonary embolism and shock (Edwards, 2003).

The excretion of calcium

The glomerulus of the kidney filters only diffusable calcium, 97–99 per cent of which is reabsorbed (Marieb, 2004). Reabsorption is predominantly
passive. Approximately 80 per cent of the calcium excreted in urine is complexed, as ionised calcium is more readily reabsorbed. PTH is the main regulator of renal calcium reabsorption.

In the kidney, calcium has several deleterious effects. It lowers the renal concentrating ability by inhibiting the response to anti-diuretic hormone and reducing medullary tonicity, resulting in polyuria and polydipsia with a low urine-specific gravity and nephrogenic diabetes insipidus. This is a disorder characterised by the kidney’s inability to respond to the anti-diuretic hormone vasopressin. The proper amount of water cannot be absorbed and is instead voided in the urine leaving the patient in danger of dehydration.

Renal failure
Patients with hypercalcaemia often present with renal failure due to renal tubule damage. This is due to a decreased glomerular filtration rate from renal vasoconstriction, resulting in renal ischaemia, renal tubular dysfunction and mineralisation in the kidney. If severe this can lead to urolithiasis. Renal function should be reassessed after the hypercalcaemia’s cause has been identified and corrected.

As kidney function worsens and dialysis is needed, blood phosphate levels become higher than normal. The body, lacking a healthy kidney’s controls on phosphates levels, responds by raising serum levels of calcium. It reduces the availability of calcium for bodily processes and takes calcium from bone. Calcium then binds to phosphate and removes it from the circulation.

In chronic renal failure, total calcium is generally normal or decreased. In 10–20 per cent of cases calcium can be elevated. However, ionised calcium is normal or even decreased. The mechanism is unknown, but the general hypothesis is autonomous PTH secretion and decreased PTH degradation, reduced calcium excretion and an increase in the formation of calcium-anion complexes, which may become lodged in the renal tubules.

Hypercalcaemia should be attributed to renal failure only after other causes have been considered and ruled out.

Hypocalcaemia
The clinical manifestations of hypocalcaemia are primarily caused by an increase in neuromuscular excitability (McCance and Huether, 1997). Symptoms include confusion, paraesthesia around the mouth and in the digits, muscle spasms in the hands and feet, and hyperreflexia. Two clinical signs that may be positive are:

- Chvostek’s sign – a twitch of the nose or lip when the facial nerve just below the temple is tapped;
- Trousseau’s sign – contraction of the hand and fingers when the arterial blood flow in the arm is occluded for five minutes.

Severe symptoms include convulsions and tetany, a continuous severe muscle spasm that can interfere with breathing and cause death. Intestinal cramping and hyperactive bowel sounds also may be present because hypocalcaemia affects the smooth muscles of the gastrointestinal tract. The characteristic electrocardiograph change in hypocalcaemia is a prolonged Q-T interval, indicating prolonged ventricular depolarisation.

The most common causes of hypercalcaemia are hyperparathyroidism, bone metastasis and calcium reabsorption from breast, prostrate and cervical cancer, sarcoidosis and excess vitamin D (McCance and Huether, 1997).

Many tumours make PTH and increase serum calcium. Many symptoms are non-specific and relate to loss of cell membrane excitability, including fatigue, weakness, lethargy, anorexia, nausea and constipation. Impaired renal function often develops and kidney stones form as precipitates of calcium salts (Yucha, 2004). A shortened Q-T segment and depressed T waves may be observed on the ECG.

### References

