POTASSIUM IN THE PERIOPERATIVE PERIOD

R. S. VAUGHAN

Potassium ions play a vital role at a cellular level. These ions are actively transported into cells, causing an electrical imbalance and a build up of potential energy. When this energy is released following correct stimulation, the cells perform their designated functions. When these functions relate mainly to the heart and skeletal muscles, nerve and renal activity, the importance of potassium in cell function becomes very clear indeed.

The excitability of the cells is proportional to the ratio of intracellular to extracellular potassium concentrations [8, 29]. Consequently, any variations in this ratio will affect cellular function, result in dysfunction of excitable cell membranes and cause the signs and symptoms [39] that are associated with imbalances of potassium concentration.

NORMAL POTASSIUM HOMEOSTASIS

The average normal body intake of potassium is about 1 mmol kg\(^{-1}\) day\(^{-1}\). Most of the potassium ingested is absorbed in the small intestines and redistributed around the body, where the main reservoir is the skeletal muscles. Approximately 90% of the total amount of potassium absorbed each day is excreted by the kidney, mainly at the distal convoluted tubules, in exchange for either sodium or hydrogen ions. This exchange is influenced predominantly by aldosterone [29].

Excretion of aldosterone from the adrenal glands is directly proportional to the serum concentration of potassium. A high concentration will lead to an increased secretion of aldosterone, and vice versa. This relationship is unaffected by sodium balance and renin concentrations. Although the function of aldosterone is related mainly to the renal aspects of potassium homeostasis, it has a secondary action in that it increases the uptake of potassium ions by skeletal cells [7].

There are also extrarenal mechanisms involved in the control of the serum concentration of potassium. Insulin induces potassium to enter the cells; this is independent of glucose uptake. Further, if the serum concentration of potassium increases greatly, additional insulin may be secreted from the pancreas. There is also evidence that there is a critical minimum concentration of insulin required for the normal uptake of potassium by cells [7].

The liver also has a modulating action. As the portal circulation drains into the liver, increased concentrations of insulin can have a significant effect upon subsequent serum concentration of potassium, causing potassium ions to move into the liver cells thus reducing the serum concentration. This relationship between the pancreas, the portal circulation and the liver provides one of the important mechanisms involved in the normal daily control of serum potassium [16].

It is not surprising, therefore, that occasionally after liver transplantation, there may be a significant increase in the serum concentration of potassium after the transplanted organ has been connected to the recipient's circulation [16]. However, recent developments in technique have enabled liver surgery to proceed without such an increase in serum potassium [12].

Membranes containing the enzyme sodium—potassium ATPase are also important modulators of potassium balance. This enzyme pumps potassium into the cell and sodium out [33]. There are several factors which can affect the action of this enzyme. One of the most important is the activity of the sympathetic nervous system [27].

KEY WORDS

Beta-adrenergic agonists and α-adrenergic inhibitors encourage potassium ions to enter the cell; β-antagonists and α-agonists have the reverse action. It has been suggested also that the serum concentration of magnesium affects the action of sodium–potassium ATPase.

Finally, the plasma pH also influences potassium homeostasis. During episodes of acidosis, hydrogen ions enter the cell and are exchanged for potassium ions, causing an increase in serum concentration of potassium. During an alkalotic period, the reverse occurs [30].

**POTASSIUM IMBALANCE**

There are two main clinical conditions associated with potassium imbalance which affect the anaesthetist, namely hyperkalaemia and hypokalaemia. However, whichever clinical condition the anaesthetist faces, acute changes in potassium concentrations present the greatest hazards. Chronic changes are far less dangerous and are managed more easily.

**Hypokalaemia**

It would appear that the clinical picture associated with hypokalaemia does not usually occur until the serum concentration of potassium decreases to less than 3.5 mmol litre⁻¹. Thereafter, the electrical activity of the heart may alter and the heart become susceptible to arrhythmias, and in particular to the effects of digitalis [18]. The classical ECG leads may show S–T segment depression, flattened T-waves, U-waves, tachycardia and eventually ectopic beats. In addition, the compensatory mechanisms which normally follow the Valsalva manoeuvre [39] are depressed also. Thus postural and perioperative hypotension can occur and may need additional therapy for correction.

Skeletal muscle weakness may also occur and this could, in the long term, be followed by the release of muscle protein into the blood. These complications may cause early respiratory and long-term renal failures. Rarely, when the serum concentration of potassium decreases to very small values, only the diaphragm and the cranial nerves function: this can present as dyspnoea, with the so-called fish mouth breathing picture [39]. The gastrointestinal system is also affected, with a generalized decrease in function. This delays gastric emptying and causes a decrease in the release of insulin.

The major cause of hypokalaemia is loss of potassium from the body. Vomiting and diarrhoea cause considerable losses. Renal losses occur following excessive diuretic therapy without additional potassium therapy, with the loop diuretics producing a greater loss than the potassium sparing diuretics; diabetes mellitus and alkalosis may have the same effect. Hypokalaemia occurring in patients receiving β₂-adrenergic agonists, xanthines and steroids has been recorded with increasing frequency [6]. Of the 26 reports received by the Committee on Safety of Medicines, four were associated with cardiac arrest. Rarer causes of hypokalaemia include Cushings syndrome, nephrosis and cirrhosis.

The main question that the anaesthetist needs to ask is: *What is the minimum safe recommended serum concentration of potassium at which routine or emergency anaesthesia may be undertaken?* The general consensus of opinion used to be about 3.5 mmol litre⁻¹, although there is now evidence to suggest that 2.5 mmol litre⁻¹ may be acceptable [38]. Despite this evidence, most anaesthetists faced with a hypokalaemic patient in the preoperative period would set up an infusion containing potassium. However, this concept does not find universal support, as Hirsch and colleagues [13] found no major problems in patients with a serum concentration of potassium less than 3 mmol litre⁻¹. The problems that did arise, namely cardiac irregularities, were associated more with previous congestive cardiac failure or long-term digoxin therapy.

The recommended maximum rates of infusion of potassium are 10–20 mmol h⁻¹, with a maximum of 500 mmol 24 h⁻¹. Further, the potassium should be infused from a pre-set pumping device and should enter the blood stream utilizing a "piggy-back" technique. Concentrated solutions of potassium given directly into a peripheral vein may cause local reactions, pain and ultimately phlebothrombosis. Large concentrations have also caused cardiac arrest [40]. It should be noted also that it may require up to 2 days to replenish body losses completely.

**Hyperkalaemia**

The clinical indications of hyperkalaemia are a decrease in the excitability of cardiac muscle, weakness of skeletal muscle and an increase in the release of insulin. The most dangerous effect of hyperkalaemia is on the myocardium. There would appear to be a threshold concentration of
approximately 7 mmol litre\(^{-1}\) at which arrhythmias start to occur [35]. If the potassium concentration increases rapidly, there is an added risk of decreased cardiac output, ventricular fibrillation or asystole. Increasing concentrations are associated with characteristic sequential changes on the ECG: appearance of tall, peaked T-waves, followed by absence of P- and diminished amplitude of the R-waves, a widened QRS complex terminating in a biphasic QRST. Ventricular fibrillation or asystole may then occur.

The major causes of preoperative hyperkalaemia are renal failure and iatrogenic events. The latter have included accidental potassium overdose [40], the infusion of triple strength plasma [41] and the transfusion of outdated blood [21] with a concentration of potassium greater than 30 mmol litre\(^{-1}\). More unusual causes include pseudohyperkalaemia and the changes which follow tissue damage and hypoxia [35].

More recently, the use of angiotensin converting enzyme (ACE) inhibitors has been implicated in the occurrence of hyperkalaemia [9]. In essence, ACE inhibitors reduce the concentration of angiotensin II and hence the production of aldosterone. The serum concentration of potassium may therefore increase, particularly when the efficiency of renal function is decreased. If the ACE inhibitor itself has caused renal failure, hyperkalaemia may become dangerous. ACE inhibitors may also cause hyperkalaemia when administered concurrently with other diuretics.

The treatment of hyperkalaemia in the preoperative period includes the use of resonium cation exchange resins, peritoneal dialysis, haemofiltration and haemodialysis [5]—for example, rectal or oral resonium if the serum concentration of potassium is increasing but has not exceeded 6.0 mmol litre\(^{-1}\). The dose of calcium cation exchange resonium would be 15–30 g repeated 6-hourly if necessary. If the serum concentration of potassium has increased to more than 6.0 mmol litre\(^{-1}\), constant ECG monitoring is mandatory and glucose 50 g and insulin 12 u should be given i.v. This therapy should continue until dialysis is provided. If overt arrhythmias occur during this period, 10% calcium gluconate 10 ml (maximum dose 50 ml) and sodium bicarbonate may be given [D. J. Fisher, personal communication], although these agents must be administered through separate i.v. cannulae.

Renal transplantation offers the best long-term solution to the artificial control of the serum concentration of potassium. However, rapid decreases in serum concentration of potassium may reveal toxic symptoms related to other therapeutic agents, for example arrhythmias associated with cardiac glycosides.

**Premedication**

There is very little evidence available to indicate that any of the agents used commonly for premedication cause any acute changes in the serum concentration of potassium. However, recently it has been shown that preoperative anxiety causes a small decrease in serum potassium concentration [19]. It is possible that anxiety causes an increase in the concentration of endogenous catecholamines which, in turn, reduces the serum concentration of potassium, probably by stimulation of sodium–potassium ATPase. Suitable anxiolytic premedication would be expected to prevent such changes.

In an anxious patient, however, a combination of hypokalaemia, increased plasma concentration of adrenaline and administration of a volatile agent such as halothane might be expected to cause arrhythmias during induction of anaesthesia.

**Induction of anaesthesia**

Induction of anaesthesia in the presence of a low serum concentration of potassium rarely causes difficulties. The evidence suggests that, providing \(P_{\text{aCO}}\) remains normal, some intracellular movement occurs. However, if the \(P_{\text{aCO}}\) is greater than normal, the serum concentration of potassium increases slightly.

The most serious problems are caused by an acute increase in serum concentration of potassium. In normal patients, suxamethonium chloride 1 mg kg\(^{-1}\) i.v. causes the serum concentration of potassium to increase by a maximum of 1.0 mmol litre\(^{-1}\) [2]. There are several conditions, however, in which i.v. suxamethonium may cause sudden and very dangerous increases in the serum concentration of potassium, as a result of a massive outflow of intracellular potassium. Although the increase may not occur at the first exposure to suxamethonium, it may follow subsequent use. The major cause of this outflow seems to be cell membrane hypersensitivity [11], the exact duration of which is generally unknown. The main conditions [17] associated with i.v. suxamethonium and hyperkalaemia are as follows:
**Burns.** It has been recommended that suxamethonium is used on the first occasion but not thereafter [28]. Others have argued that suxamethonium-induced hyperkalaemia occurs only during the first 18–66 days after a burn [10]. However, this is by no means universally accepted.

**Major trauma.** A group of patients with major trauma were compared with another control group of normal patients [23]. The increase in serum concentration of potassium associated with suxamethonium in the first group was significant and dangerous, reaching, in some subjects, approximately 9.5 mmol litre\(^{-1}\).

**Tetanus.** A significant increase associated with cardiovascular changes has been reported [17].

**Muscle dystrophies.** Observations similar to those in patients with tetanus have been recorded [34].

**Paraplegia.** The course is similar to that seen in burned patients. There is a short safe period, followed by a period of increased risk from about 14–28 days [32].

**Cerebrovascular accidents.** The course with these conditions is similar to that associated with burns patients and lasts at least 6 months [31, 37].

**Uraemia.** If the serum concentration of urea is increased in association with increased serum potassium, the use of suxamethonium is contraindicated [25]. There is no similar consensus when the concentration of urea is increased but that of potassium is normal.

**Miscellaneous conditions.** Congenital cerebral palsies, upper motor neurone disease and pseudo hypertrophic muscular dystrophies have all been associated with suxamethonium-related hyperkalaemia [35].

It would seem prudent to avoid the use of suxamethonium in all these conditions, but there may be circumstances in which suxamethonium would have considerable advantages—for example in a patient with a full stomach requiring emergency surgery. Here the anaesthetist is faced with a dilemma. If it is felt that advantages gained by the use of suxamethonium outweigh the disadvantages, what pharmacological strategies might the anaesthetist devise in order to prevent an increase in the serum concentration of potassium?

Some workers have advocated the use of a small pre-dose of a non-depolarizing neuromuscular blocker, but the efficacy of this manoeuvre has not been proven. One of the most interesting methods, proposed by James, Cork and Dennett [14], has been to pretreat patients with magnesium sulphate. Two groups of 10 patients received either i.v. saline or magnesium sulphate 60 mg kg\(^{-1}\). The serum concentration of potassium was measured after administration of suxamethonium 1.5 mg kg\(^{-1}\) i.v. In control patients the serum concentration of potassium increased by an average of 0.57 (±0.2) mmol litre\(^{-1}\), while in the magnesium sulphate group the increase was 0.05 (0.02) mmol litre\(^{-1}\) (a statistically significant difference).

How might magnesium sulphate exert such an effect, since the intubating conditions were the same in both groups? It is possible that magnesium sulphate itself causes muscle paralysis or prevents muscle from contracting (it is known that large concentrations antagonize the movement of calcium ions into the cell), and that magnesium prevents potassium efflux from the myocardial cells (as observed in isolated rat hearts).

The use of magnesium sulphate has not yet been fully investigated in patients known to be at risk from suxamethonium-induced hyperkalaemia, but has potential.

If an anaesthetist notices the classical sequential ECG changes associated with hyperkalaemia after i.v. suxamethonium, what therapeutic options are available? Either the effects of potassium on the myocardium may be antagonized, or the potassium may be redistributed into the cells [37]. Whichever method is used, immediate hyper-ventilation with increased concentrations of oxygen is also required because alkalosis encourages potassium ions to enter the cells.

Calcium chloride is the most commonly available treatment for acute hyperkalaemia. Slow i.v. injection of 10% calcium chloride 10–20 ml, using direct ECG control, usually restores myocardial excitability within 1–2 min. This effect may persist for up to 20 min.

The drug most easily available for the promotion of intracellular redistribution of potassium is sodium bicarbonate given i.v. at a dose of approximately 1 mmol kg\(^{-1}\). The effect of a bolus dose is maximal at about 5 min, but then declines rapidly. It must be remembered, however, that calcium salts and bicarbonates should not be mixed together, as calcium bicarbonate is formed.

In the longer term, glucose with insulin is a preferred regimen but, in an average operating theatre, this combination may take around 10 min to prepare. Vitez [37] has recommended an
immediate i.v. injection of 50% glucose 50 ml plus insulin 10 u. A maintenance solution of 10–25% glucose with insulin 1 u per 2 g of glucose is infused at 300–500 ml h⁻¹ and sustained for at least 6 h.

Finally, there is evidence that β²-adrenergic agents [36], particularly adrenaline, are effective in rapidly reducing the serum concentration of potassium. This technique is not used commonly in the United Kingdom.

Maintenance of anaesthesia

Factors which were important during the induction of anaesthesia continue to influence serum concentrations of potassium during anaesthesia. Once again, changes associated with hyperkalaemia are particularly important and dangerous in the maintenance phase.

Most dangerous is the development of malignant hypertonic hyperpyrexia [22]. This syndrome is triggered usually by exposure to fluorinated hydrocarbons, suxamethonium or a combination of both. Although the main thrust of treatment consists of i.v. dantrolene, oxygenation and cooling, the serum concentration of potassium does increase quickly and must be treated as discussed earlier.

Hypoxia and increased plasma concentrations of catecholamines also cause hyperkalaemia, probably as a result of decreased membrane stability and losses from hepatic cells [35].

Accidental or therapeutic hypothermia may cause hyperkalaemia. In addition, hypothermia renders the myocardium more sensitive to the action of an increased serum concentration of potassium [35].

Finally, some anaesthetists inject various substances relatively quickly. Some substances, such as penicillins, are potassium salts. It may therefore be prudent not only to inject a small amount as an initial test dose, but also to inject the remaining solution slowly.

The major factor that has, in the past, caused acute hypokalaemia has been an extracorporeal circulation [20]. This has been associated also with a metabolic acidosis and delayed insulin response [3]. However, many centres now utilize a cardiopulmonary solution to arrest the heart in diastole [22]; this solution contains large concentrations of potassium and generally prevents the occurrence of hypokalaemia traditionally associated with an extracorporeal circulation.

Acute or chronic hypokalaemia in the main-

tenance phase of anaesthesia may cause muscle weakness and intermittent positive pressure ventilation is recommended. If neuromuscular blocking drugs are used, it seems advisable that the loading doses of non-depolarizing agents should be reduced and neuromuscular transmission checked repeatedly with a nerve stimulator. Any subsequent doses should be smaller than normal and governed by the results obtained with the nerve stimulator. It would also seem reasonable that, if hypokalaemia is present, $P_{a_{CO_2}}$ should be maintained within the normal range.

Postoperative period

Acute hyperkalaemia occurs very rarely in the postoperative period. However, it has been associated with renal failure, iatrogenic causes and after liver and renal transplantation [15].

Hypokalaemia is far more common. This may cause difficulties in reversing non-depolarizing neuromuscular block and, occasionally, cardiac irregularities and hypotension. It may be that a prolonged period of artificial ventilation may be required until the serum concentration of potassium is restored to the normal range, cardiac arrhythmias disappear and full muscle power returns.

It has been calculated that potassium loss is about 100 mmol day⁻¹ for the first 2 days after surgery [26]. Thereafter, on average, the loss is 24 mmol day⁻¹, but this may increase following adrenal or bowel surgery. These losses should be replaced. The quantities of potassium required should be governed by the results of laboratory investigations, but does not normally exceed 15–20 mmol h⁻¹ or approximately 500 mmol per 24 h.

LOCAL ANALGESIA

Generally, it would seem that the actions of local anaesthetic agents are unaffected by variations in serum concentration of potassium. However, in a small series of patients, continuous extradural analgesia has been associated with reduced loss of potassium in the postoperative period [4].

Some local anaesthetic preparations include potassium salts to potentiate their actions [1]. This combination has caused oedema in the area surrounding an injection site. Further, there is some evidence that, after infiltration of local anaesthetics for dental surgery, some changes occur in serum concentration of potassium [24].
POTASSIUM IN THE PERIOPERATIVE PERIOD

There is no evidence as yet that continuous extradural infusion of opioids has any effect on potassium concentrations.

CONCLUSION

Potassium ions have an important role in the biology of man. Variations between intracellular and extracellular concentrations may affect many cellular functions. Acute changes in potassium concentrations may be very dangerous and occasionally lethal. The role of these ions in anaesthetic practice mirrors these statements.

REFERENCES


