THE MANAGEMENT OF IONIC DISORDERS WITH CARDIAC REPERCUSSION

MANAGEMENTUL TULBURĂRILOR IONICE CU REPERCUSIUNE CARDIACĂ

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ABSTRACT | REZUMAT

Ionic disorders with pathogenetic involvement in the cardiovascular system in veterinary medicine has become a subject of interest due to the increased possibilities of paraclinical testing, the diagnosis, the therapeutic management and the efficiency of the administered drugs.

Dietary and medicinal management in the subsequent disorders of ionic disorders refers to both emergency treatment by promptly correcting the expressed disorders but also by maintaining supplementation and diet.

Keywords: ionic disorders, cardiac, management

Tulburările ionice cu implicare patogenetică în sistemul cardiovascular, în medicina veterinară, a devenit un subiect de interes, datorită creșterii posibilităților de testare paraclinică, stabilirea diagnosticului, a unui management terapeutic, dar și a gradului de eficiență a medicamentelor administrate.

Managementul dietar și medicamentos în afecțiunile consecutive unor dereglări ionice vizează atât tratamentul de urgență prin remedierea promptă a tulburărilor exprimate cât și menținerea printr-un tratament de suplimentare și dietă.

Cuvinte cheie: tulburări ionice, cardiac, management

HYPERPOTASSEMIA

Normal serum potassium levels range from 3.5 to 5.5 mmol/l. Any increase over this value is known as hyperkalemia.

Etiology

Iatrogenic hyperpotassemia and spontaneous hyperpotassemia may be distinguished.

Iatrogenic hyperpotassemia

The causes of this type of iatropathy are drug and dietetic and it can be produced by three mechanisms:

1. An overdose of medicines containing potassium or managing them too quickly.

2. Drugs that cause inhibition of transcellular potassium transfer. These include alpha-agonists, succinylcholine, arginine and digitalis (overdose). Medicines that overdose lead to prolonged decubitus (barbiturates, narcotics) may also be the cause of hyperpotassemia (rhabdomyolysis as a result of decubitus).

3. Drugs that reduce urinary potassium excretion. The main ones are potassium-sparing diuretics (spironolactone, triamterene,amiloride),converting enzyme inhibitors, nonsteroidal anti-inflammatory drugs, mitotane (overdose), heparin, lead (in chronic poisoning), progesterone (aldosterone antagonists) [8].

Spontaneous hyperpotassemia

Spontaneous hyperphotassemia has the same mechanisms as those previously described:

1. Cellular potassium transfer disorders due to an insulin deficiency, a massive tissue loss (mesenteric infarction, tumor lysis, hemolysis, rhabdomyolysis, burns), acute acidosis (hyperpotassemia increases from 0.16 to 1.67 mEq / l when the pH decreases with 0.1 units. [1]

2. Disorders of urinary potassium excretion due to adrenal insufficiency, selective aldosterone deficiency, oliguric renal failure.

3. Pseudohyperpotassemia encountered in thrombocytosis (> 750,000/mm³), leukocytosis (> 500,000 /mm³). [8, 65]

4. Artifacts: Hemolyzed blood samples.

The most common causes of hyperpotassemia are oliguric renal failure in urethral obstructions in the cat, hypoadrenocorticism, iatrogenic causes and severe acidosis cases. [20, 39]

Clinical signs

Cardiac disorders are the most common clinical signs. Symptoms are the result of potassium effects on the cell membrane. The main distinguishing clinical signs are bradycardia, a weak femoral pulse and the presence of arrhythmias. Bradycardia is generally pre-

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sent in hyperpotassemia with a potassium level of about 7 mEq /l. The cardiotoxicity of hyperpotassemia is important because it can cause death. Hyperpotassemia is a major cause of mortality in both oliguric renal insufficiency or in hypoadrenocorticism [8, 32, 65]. Other clinical signs of hyperpotassemia are the muscular weakness. Nausea, vomiting, ileus, diarrhea or abdominal pain are also encountered. In severe hyperpotassemia, a severe weakness occurs in the posterior train and results in flaccid paralysis that can mimic a medullary disorder. The effects of hyperpotassemia on oesophageal muscles may lead to the occurrence of a mega-esophagus. [8, 32, 65]

Electrocardiographic modifications

There is no correlation between the degree of hyperpotassemia and changes on the ECG route. On the other hand, there are individual physiological variations, especially the T wave whose alteration is one of the first signs of hyperpotassemia but which is difficult to interpret because it is very variable in canine compared to human. Potassium cardiotoxicity can be altered by various factors: the rate of hyperpotassemia, various metabolic disorders (acidosis), electrolyte disturbances (hyponatremia or hypocalcemia), the existence of a underlying cardiopathy.

The chronology of the occurrence of ECG signs in experimentally induced hyperpotassemia can be divided into five levels:

1. Potassemia greater than 5.5 mEq /l. At this value increases the amplitude of the T wave which becomes tall and sharp. This is due to the increased rate of repolarization of myocardial fibers by accelerating the penetration of potassium into cells followed by increased membrane permeability to potassium (accelerating phase 3 of action potential). [5]

2. Potassemia over 6.5 mEq /l. There is a decrease in the wavelength R, the increase in QRS complex duration, R-R prolongation, ST segment depression. In this case, hyperpotassemia causes a slowing of management by prolonging the action potential and the refractory period. Atrial and junctional stages are the first affected. Grade 1 AV blocks are observed. At the ventricular level, the slowing of conduction translates into the progressive widening of the QRS complex and the diminishing of the amplitude of the R.21 wave. Alteration of conduction results in the disappearance of the T-wave morphological abnormalities encountered in less severe hyperpotassemia. [57]

3. Potassemia greater than 7 mEq /l. The ECG pathway shows a decrease in amplitude with the increase in P wavelength, elongation of QRS complexes, elongation of the R-R interval, prolongation of the QT segment. Flattening P-wave appears as a result of diminishing the excitability and conduction of the atrial floor. The extension of the ST segment is not at all constant.

4. Potassemia greater than 8.5 mEq /l. The main manifestations are bradycardia and the disappearance of the P wave leading to a synoventricular rhythm (atrial paralysis). The synoventricular rhythm corresponds to an intra-atrial block with the transmission of sinus influx directly to the AV node by specialized conduction then ventricular depolarization [9, 25]. Thus, there appears an atrial shunt in which all P waves disappear in all conventional derivations. Grade 2 or Grade 3.5 AV blocks can be added. The cat can encounter an extended QRS complex tachycardia and the disappearance of P95 waves.

5. Potassemia greater than 10.0 mEq /l. On the ECG pathway, an increase in the duration of the QRS complex with eventual replacement with a biphasic amplitude, ventricular flutter, ventricular fibrillation or asistol appears. The conduction becomes very diminished or even blocked at the level of the His beam and can therefore cause a branch block, a hemiblock, or a 2nd degree AV block (diagnosed in the absence of P-wave), or can cause an idioventricular escape rhythm or ventricular tachycardia [23]. Then the lead becomes blocked between the cells of the Purkinje network and the ventricular muscle fibers that lead to a terminal assistance, either a ventricular flutter or a ventricular tachycardia causing irreversible ventricular fibrillation.

The occurrence of changes in the electrocardiographic route is progressive and is dependent on increased intra- and extracellular potassium levels. It is thus difficult to establish a strict correlation between electrocardiographic and potassium disorders.

Some authors prefer to distinguish moderate to severe hyperpotassemia in view of the following electrocardiographic changes [5]:

- moderate hyperpotassemia: high or sharp T wave, sinus bradycardia with increased duration of the PQ interval (Q1 AV block) and the QRS complex, as well as an increase in duration and a flattening of the P wave. This P-wave disappears in the end (atrial paralysis or sinoventricular rhythm). The S-T segment has a depression.

- severe hyperphotassemia: branch block, grade 2 AV block with possibility of ventricular escape, then asystole or ventricular fibrillation.

Experimentally, when the increase in potassium is slow, the decrease in driving speed immediately leads

to an asystole. When potassium increase is rapid, cardiac disorders evolve towards bradycardia, a decrease in myocardial contractility, then to ventricular fibrillation. [17]

ECG monitoring is required in the clinical suspicion of hyperpotassemia because, in the absence of biochemical (urgent) results and when clinical signs are compatible, it allows the suspicion of hyperpotassemia and symptomatic treatment. However, caution is required because confusion with hypopotassemia (which causes all bradycardia), masked brachial arteries of ventricular extrasystoles or ventricular tachycardias secondary to other conditions may be possible. Monitoring the evolution on the ECG pathway in treatment permits observation of its efficacy. [15]

Treatment

The choice whether or not to treat hyperpotassemia should take into account the value of potassium, its rate of setting, its functional repercussions, and the nature of the underlying causes. A hyperpotassemia greater than 6.5 mEq /l with a rapid installation should be treated immediately. Performing a treatment is also required when characteristic electrocardiographic features for hyperpotassemia occur regardless of the amount of potassium. An asymptomatic animal with normal diuresis and chronic hyperpotassemia of the order of 5.5-6.5 mEq /l does not require emergency treatment at all, but the underlying cause has to be identified. In all variations, the cause of hyperpotassemia must be treated rapidly (eg, urethral obstruction, Addison's disease). [8, 14]

For treatment use:

Potassium antagonists:

- *Calcium gluconate 10%.* In significant cardiac toxicity its administration is indicated at a dose of 0.5-1 ml/kg i.v. in 10-15 minutes. The effect is immediate and lasts between 10 and 30 minutes. The amount injected should generally not exceed 10 ml and the injections may be repeated as needed. Calcium counteracts the toxic effects of potassium on the heart by restoring the difference between the resting membrane potential and the threshold potential, but does not reduce serum potassium levels. When calcium gluconate is given, heart rate should be monitored and treatment stopped in case of bradycardia. An ECG monitoring is recommended to track the therapeutic effect. Calcium gluconate is contraindicated in a digitized animal. [8, 47, 49, 65]

Agents that promote
the penetration of potassium into the cell:

- *Sodium bicarbonate*. By increasing the pH of the blood, potassium is promoted in the intracellular environment by the exchange with a hydrogen ion. Potassium transfer in the cell favors the restoration of the normal transcellular gradient thus allowing for counteraction of the cardiotoxic effects of hyperpotassemia. The use of bicarbonate has a double purpose when acidosis is associated with hyperpotassemia. In the absence of ionogram values, a dose of 0.5-3 mEq / kg i.v. within 10-30 minutes. The effect takes place in 5-10 minutes and takes 1-2 hours. Sodium bicarbonate should be used with caution in oliguria with heart failure because it can induce overload volume, and in patients with hypocalcaemia, alkalinisation of blood may worsen the signs of hypocalcaemia by lowering the calcium ion concentration. It is therefore advisable to know the state of acid-base balance and various ions before starting treatment with sodium bicarbonate. [8, 47, 49, 65]

- *Glucose / insulin solution*. Insulin causes intracellular glucose transfer, which is accompanied by that of potassium. An administration of i.v. glucagon or glucose (0.5 - 1 g/kg) stimulates endogenous release of insulin, which allows a decrease in potassium with 1-1.5 mEq/l/h. The effect takes place one hour after administration and takes a few hours. If faster results are required with a significant reduction in potassium, it is recommended to use fast-acting glucose insulin. In cat, rapid insulin is used at a dose of 0.5 IU / kg i.v. followed by administration of i.v. of a bolus of dextrose or glucose at a dose of 2 mg / IU insulin injected. In dogs, fast insulin can be used up to a dose of 1 IU / kg. Potassium is reduced in 30-90 minutes after administration. This protocol is frequently accompanied by a transient hypoglycaemia (attention to Addison's disease where hypoglycaemia is frequently present). Repetition is unnecessary because it is not accompanied by a further decrease in potassium, probably because cells are no longer able to accept potassium. An ECG allows evaluation of cardiotoxicity reduction. This insulin / glucose protocol is generally safe although it can cause hypophosphatemia with fatal consequences by consuming pre-existing phosphate. [8, 14, 47, 65]

Agents that act
by decreasing serum potassium:

- *Fluidotherapy*. Rehydration with poor potassium solutions is indicated in case of dehydration. It allows the dilution of serum potassium and the restoration of a correct renal flow, resulting in an improvement in potassium excretion (except for cases of oligo-renal insufficiency). The effect occurs in 5-15 minutes and takes several hours. [8, 47, 65]

- *Diuretics.* These can be used to increase potassium excretion by the kidneys. Thiazide diuretics are more effective than loop diuretics.

- *Food Diet*. In chronic hyperpotassemia, reducing potassium intake may help manage hyperpotassemia. Milk, vegetables and fruits should be avoided. [65]

- *Mineralocorticoids* may be used for the symptomatic treatment of hyperpotassemia, with the exception of patients with renal disorders where the distal tubules do not respond to aldosterone at all. Deoxychorticosterone acetate may be administered i.m. at a dose of 1-5 mg / dog once every 24-72 hours as needed. Fludrocortisone can be administered orally at a dose of 0.1-1 mg/dog/day. Fludrocortisone is easier to use, but high doses required to control hyperpotassemia may induce iatrogenic hyperactivity. [8,47,65]

- *Peritoneal dialysis and hemodialysis*. These techniques are the only ones that can be used in patients with acute oligo-renal insufficiency to combat severe hyperpotassemia. These treatments are generally used when other therapeutic options have failed [8, 65]. Animals that receive angiotensin converting enzyme (ACE) inhibitors and/or potassium-sparing diuretics are likely to develop hyperpotassemia. In addition, certain dietetic foods for animals suffering from heart failure are rich in potassium (143-381 mg/100 kcal) to compensate for potassium loss caused by the use of certain diuretics [21]. A monitoring of potassium during treatment with ACE inhibitors and/or diuretics is indispensable to anticipate the occurrence of hyperpotassemia.

HYPOPOTASSEMIA

Hypopotassemia occurs when the serum potassium concentration drops below 3.5 mmol /l. [31, 47]

Etiology

Hypopotassemia may result from a lack of potassium, an excessive (urinary or digestive) loss or an imbalance in the distribution between intra- and extracellular environments. [47]

- *Potassium deficiency*. Because potassium is found in significant amounts in food, only an total and prolonged anorexia can have a significant effect on serum potassium (in the absence of another mechanism that promotes potassium loss). Poor potassium specific diets may predispose to hypopotassemia or worsening secondary hypopotassemia of a different nature.

- *Excessive potassium loss*. These may be digestive, kidney or iatrogenic.

Digestive losses.

By vomiting - the potassium concentration of gastric secretions is 10-20 mEq /l and therefore the vomits are a cause of potassium loss. Through diarrhea, potassium losses are 5-15 mEq /day in humans. Severe diarrhea, and especially when it is a large intestine, can produce hypopotassemia. Potassium can also be retained in the digestive tract in case of obstructions or digestive occlusions (eg. dilatation-torsion of the stomach syndrome). [3]

Urinary losses.

Osmotic diuresis occurs in uncontrolled diabetes, in the polyuria following a resolved obstruction

Aldosterone contributes to potassium loss (in exchange for sodium preservation). Its secretion increases in sodium losses (eg diuretic administration), in hyperaldosteronism, in congestive heart failure, in nephrotic syndrome. [26, 38]

Chronic renal failure in cat.

Magnesium losses increase urinary potassium excretion and cause refractory hypokalemia to common treatments. [63]

Diuretics: The use of thiazide or loop diuretic may lead to varying degrees of hypopotassemia. The potassium depletion effect of these drugs mainly results from the increase in tubular flow and thus the passage through the potassium excretion sites.

Nephrotoxic antibiotics: Amphotericin B causes urinary potassium loss, followed by a nephrotoxic effect that increases the permeability of the renal tubules [3]. The use of mannitol, sodium chloride or sodium bicarbonate have an osmotic effect. [3]

Acetazolamide, used in the treatment of glaucoma, also exerts a potassium depleting effect. [3]

Transition of plasma potassium into cells.

Alkalosis is an important cause of hypopotassemia as a result of the passage of plasma potassium into the intracellular space through proton exchange. Administration of insulin or substances that stimulate its secretion (dextrose) also favors a rapid transfer of plasma potassium to the intracellular space [3].

Cases of periodic muscular weakness associated with hypopotaseemia comparable to familial periodontal hypopotassemia in humans have been described in Burmese cats [24].

The most common causes of hypopotassemia in the cat are decreasing order of chronic renal failure, serious infectious diseases (prolonged anorexia, digestive loss), iatrogenic causes and liver disorders. [46]

Clinical signs

The only clinically recognizable cardiac signs are bradycardia and rhythm disorders.

Other clinical signs. The major sign of hypopota-

ssemia is the appearance of a generalized muscle weakness. In the cat, there may be cervical ventroflexia and locomotor difficulties. Also, a paralytic ileus that causes anorexia, nausea, vomiting and anorexia may also be encountered. These clinical signs occur in the cat at potassium levels of 3 - 3.2 mEq / l while the dog is only observed at much lower values [47]. Severe hypopotassemia causes muscle cramps and even respiratory muscles paralysis. [32]

Electrocardiographic modifications

Hypopotassemia is less harmful to heart compared to hyperpotassemia. Changes on the ECG pathway occur when potassium levels fall below 3 mmol / l.

Electrocardiographic modifications are initially morphological: ST subdenvelation, T-wave changes that are generally lower [5], changes in U wave (ventricular repolarization), and QU spacing followed by repolarization disturbances [32], the QT segment may appear elongated when the U wave and the T wave merging. The subsequent rhythm disturbances are: supraventricular arrhythmias, AV blocks, ventricular arrhythmias (extrasystoles, tachycardia, fibrillation) [8]. These modifications in the ECG route are variable and less specific [3]. In humans, hypopotassemia is a predisposing factor for torsades de pointes (like hypocalcemia and hypomagnesaemia).

Treatment

Treatment should be started when potassium is less than 3 mmol/l, and this should be specific to the cause of hypopotassemia. In parallel with the specific treatment or if a cause hasn't been determined a support treatment is performed. The purpose of this treatment is to restore physiological potassium by avoiding the creation of hyperpotassemia. An oral potassium supplement is preferable because it is more effective, although potassium salts are often irritating to the digestive tract (diarrhea, vomiting, ulceration).

Potassium chloride is administered by i.v., the amount of potassium to be administered depending on potassium levels (Table 1) [47].

Table 1

Potassium levels (mmol/l)	(mmol/l) mmol of K + to 250 ml	Infusion rate (ml/kg/hr)
<2	20	6
2-2,5	15	8
2,6-3	10	12
3,1-3,5	7	16

The infusion rate should not exceed 0.5 mmol /kg /h. Administered s.c., potassium may be corrected more slowly, but the risk of iatrogenic hyperpotassemia is lower. The potassium concentration in the injected solution should not exceed 30 mEq/l [3]. Orally, the recommended dose is 1 - 3 mg /day for dogs and 0.2 mg /day for cats. [3]

Potassium gluconate exists in several forms: tablets, used at a dose of 2.2 mEq per 100 calories of food; solution (concentration of 20 mEq /ml), used at 5 ml for dogs once every 8-12 hours [3]; gel, used at a dose of 2-4 mEq / l. [32]

HYPERCALCEMIA

Calcemia has a very stable value in an individual's everyday life. However, there are physiological variations depending on age, gender and species. A more than 10% variation from normal is a pathological variation. Interpretation of measured total calcium must be performed in relation to albumin and proteinemia (55% of calcium is protein bound).

The best method of evaluating calcemia is the determination of ionic calcium [56]. Measurement of ionic calcium (the biologically active fraction) is a more sensitive and specific method to diagnose hypercalcemia. Hypercalcemia is when the serum calcium concentration exceeds 1.5 mmol /l (60 mg /l) in the dog and 1.38 mmol /l (55 mg /l) in the cat. Dogs and cats (increasing) have a plasma ion concentration greater than 0.025-0.1 mmol /l (1-4 mg /l) compared to older dogs. [10, 40]

Etiology

Calcemia can be increased by three mechanisms: disturbing the flow of intestinal, bone or renal calcium.

- Disturbance of intestinal calcium flow. Massive ingestion of calcium is rarely associated with hypercalcemia in a healthy individual. Increased absorption is frequently seen in many diseases associated with hypercalcemia: hyperparathyroidism, vitamin D poisoning and sometimes lymphoma. [37]

- Disturbance of flow in calcium bone. Bone resorption is increased in most animals exhibiting severe hypercalcemia as a result of osteoclastic growth. This may be the result of a systemic action due to humoral factors (parathyroid hormone, vitamin 1.25 D3, thyroid hormones), or may be associated with the local release of stimulants of osteoclastic activity (cytokine) [28]. However, the increase in bone resorption is generally insufficient to cause hypercalcemia alone due to compensatory mechanisms and especially renal mechanisms. [50]

- Disturbance of calcium in the kidney. The renal calcium homeostasis disorders play an essential role in the pathogenesis of most hypercalcemia. Hypercalcemia acts on renal tubules and causes urinary loss of sodium and water. Dehydration, like sodium depletion, causes an increase in tubular sodium and calcium reabsorption which aggravates hypercalcemia. Dehydration also causes a decrease in glomerular filtration rate. A glomerular or tubular lesion may be added which is frequently the result of prolonged hypercalcemia or is associated with the excretion of nephrotoxic substances such as Bence-Jones protein in myeloma. In primary hyperparathyroidism and in certain cancers, tubular calcium reabsorption is increased due to the effects of parathyroid hormone. [48]

A retrospective study of 71 cats with hypercalcemia revealed that the two most common causes of hypercalcemia in cat are kidney neoplasia followed by renal failure. Lymphomas and epidermoid carcinomas are the most common tumors [55]. A retrospective study of 46 dogs demonstrated the existence of lymphoma in half of the cases, and the cause of hyperkalemia the most common outside of the neoplastic origin was hipoadrenocorticism (5 dogs out of 36). [58]

Clinical signs

Cardiac clinical signs are relatively rare in domestic carnivores. In acute hypercalcemia of calcium, a bradycardia is observed in humans. A rapid and marked increase in serum calcium may result in an increase in arterial pressure due to hypercalcemia-induced vasoconstriction or due to concomitant kidney disease [27]. Independent of its causal factor, hypercalcemia can also severely affect nerve, gastrointestinal and renal function. More commonly, the severity of symptoms is dependent on the degree and how quickly hypercalcemia occurs. These symptoms are varied and unspecific. The presence of hypercalcemia is most commonly found following a biochemical examination.

The neuromuscular signs are characterized by generalized weakness and hyporeflexia and are quite characteristic of severe hypercalcemia. Central neurological manifestations range from lethargy to coma [48], and sometimes epileptiform seizures [30].

Gastrointestinal signs are characterized by constipation, anorexia, nausea and vomiting [48].

Urine signs are polyuria / polydipsia.

Electrocardiographic changes

These are inconsistent, frequently discrete and disproportionate to the importance of hypercalcemia. Rhythm disturbances are commonly seen with i.v. of calcium. The main electrocardiographic changes encountered are a shortening of the QT interval (increase of the ventricular repolarization rate) and an elevation of the segment ST10, and the P and T waves have a low amplitude. [6]

HYPOCALCEMIA

Animals with a completely diminished calcium concentration due to hypoproteinemia or hypoalbuminemia do not require any treatment because the ionic calcium concentration is normal or near normal. However, a determination of ionic calcium is recommended. When hypocalcemia is accompanied by neuromuscular signs, treatment should be started.

Acute hypocalcemia

Treatment of acute hypocalcemia is an emergency. It consists of the administration of 10% calcium gluconate (1ml = 0.46 mEq) injected at a dose of 0.5-1.5 ml/kg without exceeding 10 ml within 15-30 minutes. If the neuromuscular signs do not give up on this administration, it can be repeated without exceeding 5-10 mg/kg/h.Electrocardiographic monitoring, especially the ST24 segment, is recommended. Diluted calcium gluconate is partially diluted with an isotonic solution of sodium chloride or glucose and is administered by s.c. 10% calcium chloride can be given at a dose of 1.5-3 ml / kg i.v. lent [32].

Other calcium salts usable via s.c. or i.m. (glycerophosphate or lactate) are sometimes preferred because they are less cardiotoxic and easier to administer when the animal experiences seizures [7].

Tetanus crises are reduced to administration of diazepam. In eclampsia, is supplemented by the administration of vitamin D or its precursors. In case of relapse, it is essential to suppress lactation.

When hypocalcemia is accompanied by hyperphosphatemia (renal failure), parenteral calcium may be precipitated when the dose exceeds 4500 mg/l and thus the mineralization of soft tissues [7].

In ethane glycol intoxication, the treatment consists of calcium administration until a low calcium ionic concentration is obtained slightly below the normal level and parallel treatment of hyperphosphatemia (chelators) [7, 13]. Hypocalcemia due to calcium redistribution (anti-coagulants, bicarbonate use) responds well to a short therapy (less than 6 hours). [13]

Chronic hypocalcemia

The treatment of chronic hypocalcemia depends on its origin. Symptomatic treatment is necessary in hypoparathyroidism or in renal failure.

It is based on the administration of calcium salts (gluconate, carbonate, lactate).

Table 2

Calcitherapy

Active principle	Presentation	Calcium content	Dosage
Parenteral treatment			
Calcium gluconate	10%Solution	9,3 mg/ml	0.5-1.5 ml / kg i.v. slow or 1-2 ml / kg after dilution 1: 1 with saline for s.c.
Calcium chloride	10% Solution	27,2 mg/ml	5-15 ml/kg/h i.v.
Oral treatment			
Calcium carbonate	Tablets or pungent suspension	1 g contains 400 mg of calcium	25-50 mg/kg/day
Calcium lactate			
Calcium chloride			
Calcium gluconate	pungent suspension	1 g contains 200 mg of calcium	

Table 3

Use of vitamin D and its precursors in the treatment of hypocalcemia

Vitamin D	Dosage	Advantages / disadvantages
Ergocalciferol (Sterogyl) Uvesterol	500-200 IU/kg/day or 4000-6000 IU/kg/day initially (3-4 days) then 1000-2000 IU/kg/day or week of maintenance.	Long duration of action (5-21 days) and long duration of action (18 weeks): Difficult balancing treatment. Low costs.
Dihidrotahisterol	0.004-0.01 mg/kg/day or 0.02-0.03 mg/kg/day initially (3-4 days) then 0.01-0.02 mg/kg every other day or once every 2 days.	Short action period (1-7 days). Short duration (1-3 weeks).
Calcitriol (Rocaltrol)	0.03-0.06 µg/kg/day or 20-30 ng/kg/day initially (3-4 days) then 5-15 ng/kg/day for maintenance.	Short action period (1-4 days). Short duration (2-7 days). High costs.

When calcium intake is much higher than normal, calcium absorption occurs despite the absence of calcitriol [4]. This is a passive phenomenon. To restore active calcium absorption, direct vitamin D intake in the form of calcitriol is considered as reference treatment [4, 18]. Among the vitamin D precursors are ergocalciferol, dihydrotachisterol and 1-alpha-hydroxycolecalciferol or alfacalciol which is the only one that doesn't undergo any renal hydroxylation. There is little data on their use in dogs. [4, 8, 43]

Administration of thiazide diuretics used in human medicine reduces urinary calcium elimination but this effect has not yet been demonstrated in the cat and is controversial in dogs (Tables 2 and 3). [4, 54]

HYPERMAGNESEMIA

The usual magnesia values in dogs vary slightly between different authors: from 1.89 to 2.51 mg /dl (0.78-1.03 mmol /l) 81 and from 1.7 to 2.4 mg /dl (0.70-0.99 mmol/l) [12]. In the cat, the recommended values of some authors are 1.8-2.5 mg /dl (0.74 - 1.03 mmol /l) [12]. Plasma Magnesium exists in three forms: ionic (70%, biologically active), protein-bound (20%) and complex, especially phosphate and citrate (10%). The usual levels of ionic magnesium concentration in the literature are 1.07-1.46 mg /dl (0.44 - 0.60 mmol /l) in the dog. [12]

Hypermagnesemia is a uncommon ionic disorder, taking into account the kidney's ability to increase the

removal of magnesium in the event of a higher intake. Causes of hypermagnesemia are renal insufficiency, disendocrinia and iatrogenic intakes.

Clinical signs

Cardiac manifestations are a consequence of slowing intracardiac conduction and decreasing the frequency of the sinoatrial node[1]. Distinctive clinical signs are bradycardia, hypotension and conduction disorders that can lead to terminal ventricular fibrillation [34]. Other non-cardiac clinical signs are neuromuscular (hypermagnesemia alters synaptic transmission by alteration of acetylcholine action) [42, 52]. The first remarkable clinical sign is the reduction of tendon reflexes. In extreme hypermagnesemia, the blockage of the nerve influx can cause respiratory muscles paralysis and death [42]. In severe hypermagnesemia, disturbances of the vegetative nervous system are manifested by vascular collapse. [2]

Electrocardiographic changes

Of these, the most important are prolonging the PQ interval, increasing the duration of the QRS complex. These electrocardiographic signs are observed when the magnesia exceeds 2.5 mmol/l [34]. The cardiac frequency increases initially, then decreases. In humans, the cardiac arrest occurs when the magnesia reaches 12.5 mmol/l. These changes occur as a result of a decrease in ion channel conduction of the sinoatrial node and the AV node and the alteration of the acetylcholine cholinergic receptor sensitivity. Prolongation of the PQ interval may occur due to a block of calcium pumps. Because repolarisation is poorly affected by hypermagnesemia, QT interval duration is not altered. [44]

Treatment

Treatment when patient status is stable. When kidney function is not altered at all, the increase in diuresis by the use of diuretics in fluidtherapy (0.9% NaCl solution) is the primary therapy. In severe impairment of renal function, treatment for the reduction of magnesium is by dialysis. [34]

Table 4

Therapeutic agents used in hypermagnesemia

Substanța activă	Doza
NaCl 0.9%	100-125 ml/kg i.v.
Furosemide	2-4 mg/kg at 12-24 h
Calcium gluconate	5-15 mg/kg i.v. slow
Physostigmine	0,02 mg/kg at 12 h i.v.

Emergency treatment

In the case of severe hypermagnesemia accompanied by a respiratory arrest, intubation is recommended with assisted ventilation and administration of a calcium gluconate injection [2, 53, 59]. Calcium is a magnesium antagonist at the neuromuscular junction and allows to limit the cardiotoxic effects of the hypermagnesemia. Adrenaline and noradrenaline are usually ineffective [41]. Anticholinesterases may be administered to combat the neurotoxic effects of hypermagnesemia (Table 4) [42, 34].

HYPOMAGNESEMIA

Hypomagnesemia occurs when the magnesium concentration is lower than usual.

Etiology

Hypomagnesemia is more common than hypermagnesemia. A hypomagnesaemia can occur through three mechanisms: a decrease in intestinal absorption of magnesium, an increase in urinary excretion, or a redistribution of magnesium. [13]

- Hypomagnesaemia of intestinal origin.

A decrease in food intake (prolonged anorexia) or all diseases that cause a decrease in intestinal absorption (pancreatic insufficiency, enterectomy, inflammatory bowel disease) can cause hypomagnesaemia. However, clinical repercussions of this type of hypomagnesemia are very rare in veterinary medicine. [13, 33]

- Hypomagnesemia of renal origin.

Renal loss of magnesium plays a predominant role in the development of hypomagnesemia. All tubular affections cause a significant loss of magnesium. Hyperthyroidism and hypoparathyroidism contribute to the development of hypomagnesemia. Renal magnesium excretion is increased in, hypophosphatemia, osmotic diuresis induced by hyperglycemia or mannitol.

- Hypomagnesemia by redistribution.

Insulin causes a transfer of magnesium from the extracellular medium to the intracellular environment. The massive release of catecholamines in the body's intense stress (sepsis, trauma, hypothermia) can also lead to this type of transfer.

Clinical signs

Hypomagnesemia causes an increase in myocardial excitability. The main cardiac sign on hearing is a rhythm disorder [13]. Other clinical signs encountered may be a direct consequence of hypomagnesemia or secondary to hypopatassemia which are ionic disorders commonly found in animals in hypomagnesemia [36]. Clinical signs appear primarily as a result of in-

creased neuromuscular excitability followed by an increase in acetylcholine release in nerve junctions and intracellular calcium growth in skeletal muscles [62]. Concomitant hypokalemia may result in muscle weakness, dysphagia or dyspnoea. When hypomagnesemia is accompanied by hypocalcemia, muscle tremors, ataxia or seizures. In dogs receiving a deficient magnesium regimen, hyperexcitability followed by seizures may occur after one month.

Electrocardiographic changes

Electrocardiographic changes in experimental hypomagnesemia in the dog have been studied several times. They generally occur when the magnesia drops below 0.8 mg /dl (0.33 mmol /l) [45]. Changes most commonly encountered are a sharp T wave and a slight depression of the ST segment [45, 60, 61]. T wave changes occur when hypopatassemia occurs. It does not appear to be directly attributable to hypomagnesemia. These electrocardiographic changes only occur when signs of magnesium depletion have been present for several weeks.

Treatment

Several clinical studies have shown that the mortality rate is increased in animals with hypomagnesemia [12, 35, 36]. A magnesium supplement is recommended when the magnesia drops below 1.2 mg /dl (0.49 mmol /l) or when the clinical signs are present. In moderate hypomagnesemia, the treatment of the cause is generally sufficient [13]. Magnesium should not be administered to a patient with cardiac or renal impairment (the dose may be reduced by 50-75%). Magnesium is also contra-indicated in myasthenia [29].

Emergency treatment

The purpose of this treatment is to eliminate the clinical signs. Magnesium is administered via i.v. in the form of sulphate (8.13 mEq / g) or chloride (9.25 mEq /g). The recommended dose is 0.75-1.0 mEq /kg /day in infusion. Plasma magnesium restoration is slow, and i.v. should be continued with an oral supplement (0.3-0.5 mEq/kg/day) for 2 to 5 days [11]. Magnesium sulphate is the most widely used. When hypomagnesemia is associated with serious ventricular rhythm disturbances, a magnesium dose of 100 mg /kg may be administered i.v. slow (in 5-15 min). [11]

A daily determination of magnesium is recommended during supplementation to avoid the occurrence of hypermagnessemia generally associated with hypocalcemia [13].

Treatment in chronic hypomagnesemia

It is interesting to recommend magnesium supplementation to those dogs receiving long-term treatment based on digoxin and furosemide. The recommended dose is 1-2 mEq/kg/day of oral magnesium. The main unwanted effect is diarrhea. [13]

HYPOPHOSPHATEMIA

Usual levels of phosphatase are 2.5 - 6 mg /dl (0.8 - 1.9 mmol/l) [51]. Hypophosphatemia is considered to be moderate if it is between 1 and 2.5 mg /dl (0.32 and 0.8 mmol/l). It is therefore asymptomatic.

When phosphatemia falls below 1 mg/l (0.32 mmol /l), hypophosphatemia is severe [32].

Hypophosphatemia is most commonly associated with a chronic phosphate depletion. [22].

Etiology

Hypophosphatemia and phosphate depletions can occur through three mechanisms: an increase in urinary excretion of inorganic phosphate, a decrease in intake or digestive loss, an inorganic phosphorus transfer from the extracellular medium to the cells:

The most common causes of severe hypophosphatemia are aceto-acidosis, respiratory alkalosis and renegade syndrome. [19]

Clinical signs

Hypophosphatemia may be the cause of haematological disorders (haemolytic anemia, decreased leukocyte function, thrombocytopenia), bone (osteomalacia), neurological (tremors, ataxia, convulsions, coma), kidneys (reduction of reabsorption of bicarbonates leads to acidosis).

Treatment

Asymptomatic animals in moderate phosphate-deficient hypophosphatemia and those with phosphatemia greater than 1.8 mg dl generally do not require any additional phosphorus. Phosphate supplementation is indicated in symptomatic animals and in asymptomatic animals when the development of symptomatic hypophosphatemia (eg cat with keto-acidosis diabetes with a phosphatamycide of 1.6 mg/dl) is susceptible. The required dose and response quality are very variable from one patient to another. [64]

In cases of severe hypophosphatemia, supplementation should be by i.v. with potassium or sodium phosphate (depending on ionogram) diluted in glucose 5% or 0.9% NaCl. The recommended dose is 0.03-0.06 mmol/kg/h in slow infusion over a 6-12 hour period. Phosphatemia should be measured once every 6-12 hours. In the case of chronic hypophosphatemia, intake of phosphates in food can be proposed. The recommended dose is 1-2 g of phosphorus per day [7]. Daily dose fragmentation improves digestive tolerance and intestinal absorption and avoids diarrhea.

HYPERPHOSPHATEMIA

Hyperphosphatemia is when phosphatase exceeds 6 mg /dl (1.92 mmol /l).

Etiology

The main causes are chronic kidney failure, acute renal failure, vitamin D intoxication and tumor lysis syndrome (acute leukemia, lymphoma). [16, 32]

Clinical signs

Hyperphosphatemia is frequently asymptomatic. The clinical and biological signs that are associated depend on the context in which it occurs. A rapid increase in phosphatase is generally accompanied by a decrease in serum calcium that causes its own symptomatology. When phosphatamia is increased in a sustained manner, the initial decrease in serum calcium is corrected by compensatory mechanisms. An acute hyperphosphatemia may be suspected in the case of signs of hypocalcemia. When it is chronic, it may participate in certain clinical signs: vomiting, diarrhea, cardiac conduction disorders, soft tissue calcifications (vessels, lungs, myocardium, gastric mucosa, subcutaneous tissues, joints), kidney failure. [7, 32]

Treatment

Symptomatic treatment can be performed when there is a risk of soft tissue mineralization or clinical signs of associated hypocalcemia. The basis of treatment is to reduce food intake (protein restriction) associated with intestinal phosphate chelators.

It is mainly in the treatment of patients with advanced renal impairment. [7, 16]

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