Recommendations for treating and preventing canine parvovirus

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discuss the emergence, presentation and diagnostic techniques of this worldwide pathogen in dogs, before looking at therapy and management methods

Summary

Despite routine vaccination, veterinary practitioners are all too familiar with canine parvovirus (CPV), which is the most common cause of viral enteritis in dogs. Clinically, CPV causes haemorrhagic diarrhoea and leukopaenia – which, when untreated, can result in high mortality from sepsis as a result of intestinal bacterial translocation. Aggressive supportive therapy leads to recovery in most cases.

Despite investigations into novel treatment options, the early use of enteral nutrition, aggressive fluid therapy and antimicrobials are the only treatments shown to improve clinical outcome. Evidence also suggests a benefit to the use of recombinant interferon. Vaccination provides protection in most dogs, although interference of maternally derived antibodies can result in vaccination failure.

Key words

canine parvovirus, **vaccination**, **enteritis**, **interferon**

CANINE parvovirus (CPV) is a worldwide pathogen and remains the most common cause of canine viral enteritis in the UK.

Mortality in experimentally infected dogs – without treatment – can reach 91 per cent; however, with intensive therapy, mortality can fall to below 10 per cent (Prittie, 2004).

This article provides an overview of CPV, focusing on treatment and prevention recommendations.

Background

CPV emerged as a canine pathogen in 1978 and is thought to have arisen as a mutation of feline panleukopaenia virus.

Parvoviruses are small, non-enveloped, single-stranded DNA viruses that are ubiquitous and persistent in the environment. The original CPV-2 strain has been virtually replaced by the more virulent CPV-2a and CPV-2b strains in the UK (Decaro et al, 2007). CPV-2c is now the predominant strain in many parts of Europe and is present in the UK. There is no reported difference in virulence between strains 2a, 2b and 2c (Prittie, 2004).

CPV is transmitted by the faeco-oral route. Primary virus replication occurs in lymphoid tissue before systemic distribution. CPV has tropism for rapidly dividing cells – namely the intestinal crypt, lymphoid system and bone marrow, as well as the myocardium in the neonate.

Clinical presentation

CPV predominantly affects dogs aged six weeks to six months old, as most adult dogs are immune due to vaccination or previous mild or subclinical infection.

The severity of clinical signs depends on multiple factors including age, vaccination status, presence of maternally derived antibodies (MDA), stress factors, viral load and co-infection with other enteric pathogens. Dietary change and stress at the time of weaning and rehoming make puppies less than 18 weeks old particularly susceptible.

Disease is acute, with pyrexia, anorexia and depression, followed by vomiting and profuse diarrhoea (haemorrhagic in 50 per cent of cases; Figure 1). Severe dehydration is usually apparent on presentation.

Virus replication in the bone marrow leads to leukopaenia. The combination of leukopaenia and intestinal crypt cell destruction means there is a high risk of sepsis due to intestinal bacterial translocation and subsequent endotoxic shock. Puppies usually present collapsed, poorly perfused

and hypothermic, with possible signs of jaundiced and disseminated intravascular coagulation. Myocarditis mostly occurs in puppies less than two weeks old and is rarely reported.

Diagnosis

A tentative diagnosis of CPV can be made from history and clinical signs. Haematology reveals a leukopaenia in 50 per cent to 85 per cent of affected dogs within 72 hours of the onset of enteric signs. Hypoalbuminaemia, electrolyte abnormalities, anaemia, increased liver enzymes and hyperglobulinaemia may be seen.

Abdominal ultrasound should be considered if abdominal pain is present and to exclude an intussusception. Faecal samples to exclude parasitic and bacterial causes of diarrhoea may also be useful.

An in-house SNAP Canine Parvovirus Antigen Test (IDEXX Laboratories) is commonly used to detect faecal CPV and has a high specificity (up to 80 per cent) for strains 2a, 2b and, to a lesser extent, 2c (Decaro et al, 2010). Recent vaccination (within 15 days) with a modified live CPV vaccine may cause false positives.

SNAP tests have significantly reduced sensitivity compared to PCR or electron microscopy (Schmitz et al, 2009) and false negatives may occur due to a relatively small window of faecal viral shedding. Real-time PCR is, therefore, recommended in patients where in-house tests are negative, but a high clinical suspicion remains.

Treatment

There is no specific therapy for CPV and aggressive supportive treatment to address hypovolaemia and secondary bacterial infection is vital.

Any patient with suspected CPV should be barrier nursed – firstly to protect other hospitalised patients, but also to prevent nosocomial infection in the neutropaenic patient (Figure 2). Table 1 summarises recommended treatments.

Fluid therapy

A balanced electrolyte solution (for example, lactated Ringer’s solution) is indicated to support circulating blood volume, replace fluid deficits and ongoing losses, and provide maintenance requirements. Ideally, fluids are administered IV, but in severely collapsed and/or small patients, intraosseous fluids can be given. SC or intra-peritoneal fluids are unlikely to be effective.

Crystalloid boluses (10ml/kg to 20ml/kg over 10 minutes to 20 minutes) in shocked patients can be used to improve peripheral perfusion. These should improve perfusion, reduce the heart rate and

lead to improved pulse quality. If crystalloid resuscitation fails, slowly administered colloid boluses can be used (4ml/kg to 5ml/kg over 10 minutes to 30 minutes of small molecular weight molecules such as gelatines would be most useful).

Once hypovolaemia is corrected, crystalloids at rates to correct dehydration and provide maintenance requirements are required. Larger molecular weight colloids – such as the starches – can be used to support hypoalbuminaemic patients and should be considered if albumin levels fall below approximately 15g/L.

Hypokalaemia and hypoglycaemia are commonly present due to vomiting and anorexia, and fluids should be supplemented with potassium and glucose as required. In anaemic and hypoproteinaemic cases, whole blood, plasma or packed red blood cell transfusions may be indicated. Plasma infusions may provide passive immunity, but their benefit is, as yet, anecdotal.

Antimicrobials

Antimicrobials are warranted to control bacterial translocation across the damaged gastrointestinal barrier. Parenteral cephalosporins may be sufficient in afebrile cases, whereas four-quadrant cover with potentiated amoxicillin or a cephalosporin plus metronidazole is recommended in febrile patients or patients that are significantly neutropaenic (less than 2.5×10^9/L).

Fluoroquinolones are a broad-spectrum alternative (for example, pradofloxacin), but are relatively contraindicated in growing animals.

Antiemetics

Antiemetics improve patient comfort and increase appetite in nauseous patients, as well as reduce ongoing fluid loss. Metoclopramide administered as a constant-rate infusion is very effective in controlling vomiting and may help improve intestinal motility if ileus is present.

Maropitant is a very potent antiemetic, but its safety in dogs less than eight weeks old is not established and hypoalbuminaemic patients may require a lower dose (typically a 50 per cent dose reduction is made).

Nutrition

Traditionally, “nil per os” was promoted in CPV infections, but research has shown significant weight gain and earlier clinical improvement, as well as suggested improved gut barrier function when early enteral nutrition is provided (Mohr et al, 2003). Unless feeding exacerbates vomiting, voluntary or tube feeding (Table 2) should be commenced promptly.

Naso-oesophageal tubes are easy to place with little or no sedation. Care should be taken with

naso-oesophageal tubes in vomiting patients that the tube does not become dislodged, as aspiration pneumonia can develop.

Feeding should be little and often, or even trickle-administered if by tube. A highly digestible diet with sufficient high biological value protein and minimal fat is ideal, but any intake is desirable. A source of glutamine may also be considered, providing energy directly to the enterocytes.

Parenteral nutrition may be necessary if anorexia and/ or emesis is prolonged, but may be more feasible in a referral hospital setting.

Analgesia

Addressing abdominal pain with opioid analgesia (for example, buprenorphine) is preferable to using NSAIDs, due to concurrent dehydration and gastrointestinal compromise.

Novel therapies

Recombinant feline interferon has been shown to significantly decrease mortality and clinical signs of CPV in a study by De Mari et al (2003).

Numerous other immunotherapies have been investigated in CPV, including human recombinant granulocyte colony-stimulating factor (Rewerts et al, 1998), immune plasma (Bragg et al, 2012) and recombinant bactericidal permeability-increasing protein (Otto et al, 2001), but there is little evidence for their benefit. There is also little support for the use of antivirals, such as oseltamivir (Savigny and Macintire, 2010).

Monitoring

Patients infected with CPV are deemed critical and must be monitored closely, with treatment adjusted accordingly. In young patients with little reserved glucose and electrolyte, changes can happen quickly, thus regular clinical examination (two to four times a day) with appropriately frequent blood sampling, depending on the patient, is essential to picking up early changes and intervening before complications develop.

Vaccination

The routine use of modified live vaccines has greatly reduced CPV incidence. Vaccines are based on type 2, or type 2 subtypes, and immunity against CPV-2a, 2b and 2c subtypes has been shown. Timing of primary and booster vaccinations is a matter of debate.

The World Small Animal Veterinary Association recommends a final vaccination in puppies is given

no earlier than 14 weeks to 16 weeks old to reduce the effect of MDA (see further on). It also recognises core vaccine “boosters” are unlikely to be needed more often than every three years; 95 per cent of dogs that have not been vaccinated for three to 15 years have protective CPV titres (Böhm et al, 2004). In dogs where vaccination is undesirable (for example, due to historical adverse reactions) serum antibody titre can be measured to determine whether vaccination is required; titres greater than or equal to 1:80 are protective.

Why do vaccines fail?

Vaccination may fail due to variable protection provided by MDA. A period of susceptibility exists in puppies from six weeks old where declining MDA may allow natural infection, but also prevents an effective vaccine-induced humeral response.

Modern high-titre vaccines are designed to overcome MDA and, therefore, provide immunity before MDA wanes. Rottweilers, Staffordshire bull terriers and Dobermanns are among breeds at increased risk of infection due to suspected poor humeral responses to vaccination and increased MDA persistence (Houston et al, 1996).

Prognosis

Survival to seven days after the onset of clinical signs of CPV is associated with recovery and lifelong immunity. Survival rates of more than 90 per cent can be expected where prompt, aggressive therapy is instigated and rates are higher in tertiary referral hospitals than in first opinion practices (Otto et al, 2001).

The degree of neutropaenia is a useful prognostic factor; dogs with a neutrophil count greater than 3×10^9/L at presentation predicts survival in 95 per cent of cases (Goddard et al, 2008).

• Please note some drugs mentioned in this article are used under the cascade.

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Figure 1. A puppy with watery haemorrhagic faeces due to canine parvovirus infection.

Figure 2. A four-month-old West Highland white terrier puppy recovering from canine parvovirus. Overalls and gloves are used to barrier nurse the patient.

IV fluid therapy	Crystalloids (lactated Ringer's solution)	Initially: 10ml/kg to 20ml/kg boluses in shocked patients. Repeat up to 60ml/kg to 90ml/kg to improve perfusion. Ongoing: fluid deficit (percentage dehydration × bodyweight in kg) + maintenance requirements (50ml/kg/day, potentially more in patients weighing less than 5kg or with ongoing insatiable losses) administered over 24 hours.
	Colloids	Boluses of 5ml/kg, where required, in hypoalbuminaemic patients 10ml/kg/day to 20ml/kg/day, typically with a 50 per cent reduction in crystalloid rate.
Fluid supplementation (where required)	Potassium	Use serum potassium levels to guide (See *BSAVA Formulary*). 5mmol potassium chloride per 250ml of fluids provides maintenance potassium in anorexic patients or when potassium levels are unknown. Infusion rate must not exceed 0.5mEq/kg/hour.
	Glucose	Supplement a balanced crystalloid solution with glucose to make a 2.5 per cent to 5 per cent glucose solution.
Antibiotics	Potentiated amoxicillin Metronidazole Cephalosporin – for example, cefuroxime	20mg/kg IV every 8 hours. 10mg/kg IV every 12 hours. 15mg/kg IV every 8 hours.
Antiemetics	Metoclopramide Maropitant Ondansetron	1mg/kg/hour to 2mg/kg/hour IV constant-rate infusion, or 0.25mg/kg to 0.5mg/kg SC every 12 hours. 1mg/kg SC every 24 hours. 0.5mg/kg IV loading dose then 0.5mg/kg/hour constant-rate infusion.
Nutritional therapy	High biological protein, low-fat diet to provide resting energy requirement (RER) RER (kcals) = (bodyweight in kg × 30) + 70	Suitable diets include Hill's Prescription Diet i/d and Royal Canin Sensitivity Control. Small feeds every 2 to 4 hours.
Analgesics	Buprenorphine	0.01mg/kg to 0.02mg/kg IV, SC every 6 to 8 hours. (Full μ agonists are unlikely to be indicated and have a greater effect on gastrointestinal motility).
Interferon	Virbagen Omega – recombinant feline interferon omega	2.5 million unit/kg IV every 24 hours for up to 3 doses.

Table 1. Treatment recommendations for canine parvovirus

Tube-feeding guidelines
• Complete high-calorie liquid food (for example, Royal Canin Convalescence Support) • Stop if perpetuates vomiting • Remove tube once eating greater than 50 per cent resting energy requirement (RER) voluntarily • Tempt to eat by mouth at each feed • Daily tube (and stoma in oesophageal tubes) care
Feeding regime, split over several meals – for example, every two to four hours:
Day 1 – 1/3 RER
Day 2 – 2/3 RER
Day 3 – full RER

Table 2. Guidelines for tube-feeding patients with canine parvovirus