

ACTUALITIES IN THE THERAPEUTIC MANAGEMENT OF SALMONELLOSIS

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Abstract

Contamination of food with *Salmonella* is a serious public health concern, and Community legislation on animal health covers the control of salmonella as a food-borne zoonotic agent. However, salmonellosis is a common bacterial disease responsible for major foodborne diarrheal disease in companion animals. For this reason, in some circumstances, the stamping-out policy of *Salmonella* control is replaced by therapeutic intervention, but the use of antimicrobials is not always recommended. This paper presented the options of treatment in the food-borne diarrheal disease associated with salmonellosis in companion animals (dogs and cats). The actual concept of salmonellosis treatment in companion animals comprise symptomatic and supportive therapy, diet and client education (increasing the quality of life, restrict access to the animal, good hygiene). Diet will be adapted at particularities of each clinical case, and may involve food restriction (1-2 days) and a high digestible, low-fat diet. To increase the quality of life, the microclimate conditions should be reconsidered. Development of a treatment plan for salmonella infections aims to facilitate the application of the best therapy but especially the removal of possible errors. The form of treatment depends on the severity of illness. The symptomatic treatment consists of replacing fluid and electrolyte losses: polyionic isotonic solutions, plasma transfusions, hypertonic glucose solutions. Specific treatment is chosen after culture and susceptibility testing (DST). As a conclusion, therapeutic management of salmonellosis should be approached as a plan, following all goals and using the best antimicrobial therapy in order to control the risk of creating carrier animals.

Key words: *Salmonella*, foodborne diarrheal disease, antimicrobial therapy, supportive therapies.

INTRODUCTION

Salmonellosis is a common bacterial disease, responsible for major foodborne diarrheal disease both in humans and animals, causing significant economic losses represented by mortality, especially among birds, financial expenses for starting and maintaining prophylaxis, treatment and sanitation outbreaks (Verdes, 1995; Perianu, 2003; Hoelzer, 2011; Danes, 2011).

Contamination of food with *Salmonella* presents a serious public health concern, because is the main source of human infection (Hoelzer, 2011; Danes, 2011), and almost 94 million of human gastroenteritis with 155,000 deaths per year occur across the world (Majowicz et al., 2010). For this reason in the disease management is applied the Latin adage "prævenire melius est quam curare" (better to prevent than to cure) (WHO, 2011). According to this quote, as well as many others, prophylaxis must be given special attention by informing the public on the

importance of food hygiene and creating a safe microclimate for animals (Verdes, 1995; Danes, 2011).

Table 1. *Salmonella* serovars pathogenic to humans*

Serotype of <i>Salmonella</i>	Disease	Main animal hosts
<i>S. Typhimurium</i> ; <i>S. Enteritidis</i>	Gastro-intestinal symptoms, high morbidity, low mortality	Poultry, cattle, sheep, pigs, horses, mouse
<i>S. Dublin</i>	Enteritis, abortion, meningitis, septicaemia, osteomyelitis, arthritis, dry gangrene of the extremities	Adapted to cattle, Rare in sheep and pigs
<i>S. Choleraesuis</i> ; <i>S. Typhisuis</i>	Systemic disease, low morbidity, high mortality	Swine
<i>S. Montevideo</i>	Enteritis; Septicaemia;	Ovine
<i>S. Typhi</i>	Typhus	Humans

*after Perianu 2003, Danes, 2011, Singh V., 2013

Salmonella serotypes differ in their pathogenic potential for humans and the animals infected present variable risk for transmission to humans (Hoelzer, 2011), and control measures applied can vary from one case to another.

Cattle are main source of human infection both by indirect (contaminated food) and

direct (infected animals exposure) routes of infection. Clinically sick animals shed higher concentration of *Salmonella* and probably pose the greatest risk to humans (Wray et al. 1989; Hoelzer, 2011). Cattle salmonellosis evolves as watery or bloody diarrhea, usually associated with fever, depression, anorexia, dehydration and endotoxemia. Sometimes were recorded abortion and respiratory disease (Giles et al., 1989; Huston et al., 2002; Perianu, 2003; Danes, 2011)

Sheep can develop acute enteric salmonellosis after infection serotypes *S. Typhimurium* or *S. Dublin*. Common clinical signs in adult sheep are fever, anorexia, depression, diarrhea and abortion, while in lambs is common septicemia which can lead to death or polyarthritis, pneumonia, and severe diarrhea (Uzzau et al., 2001; Sharma et al., 2001; Danes, 2011).

Depending of the pig age at the moment of infection and the *Salmonella* serotype, animals develop different clinical forms of salmonellosis. Piglets infected with *S. Typhimurium* develop mild gastro-intestinal disease (Cote et al., 2004), while in infection with *S. Choleraesuis* develop severe systemic disease with fever, diarrhea, inappetence, depression, respiratory distress, lameness, edema, hypoxia, and high mortality rates (Boyen et al., 2008).

Clinical *Salmonella* infections among horses can evolve with profuse, watery and malodorous diarrhea with abdominal pain, fever, dehydration, depression, gastric reflux and endotoxemia with cardiovascular shock or coagulopathies (Wenkoff, 1973; Roberts and O'Boyle, 1982). Also, respiratory and systemic forms of *Salmonella* infection have been described in foals, commonly this form were associated with meningoencephalitis, arthritis, osteomyelitis, or soft-tissue abscesses (Platt, 1973; Stuart et al., 1973; Blikslager et al., 1991; Ernst et al., 2004).

Salmonella infections among dogs and cats can be manifested as enterocolitis and endotoxemia often associated with fever, vomiting, anorexia, dehydration and depression (Morse et al., 1976; Philbey et al., 2009). Also, conjunctivitis, respiratory distress, meningoencephalitis, and abortion or stillbirth have been described (Caldow and

Graham, 1998; Carter and Quinn, 2000).

Rabbit salmonellosis include enteritis, metritis, and abortion; depending of *Salmonella* serotypes involved, infection can be associated with high mortality (Agnolotti et al., 1999).

Turtles, terrapins, snakes, iguanas, bearded dragons, geckos, chameleons, and other exotic animals usually have asymptomatic *Salmonella* infection, but they are frequently linked with human salmonellosis (Woodward et al., 1997; Hoelzer, 2011)

Under certain circumstances *Salmonella* control strategy implies therapeutic intervention (e.g. pets, exotic animals, high value animals), and in others stamping-out of contaminated herd (e.g. government-backed programs of the infection control in food animals) (Verdes, 1995; Perianu, 2003; Danes, 2011).

In this paper, we review our current understanding of the therapeutic management in *Salmonella* infections.

MATERIALS AND METHODS

To understand the current concepts of the therapeutic management in *Salmonella* infections, we studied seven books of pharmacology or animal infectious diseases (Stroescu 1989a, b; Moga-Manzat, 1995; Crivineanu, 2009; Perianu 2003; Danes, 2011; Bielke et al., 2012) and sixteen scientific studies (Magallanes et al., 1993; Ruiz et al., 1999; Fey et al., 2000; Hirose et al., 2001; Aarestrup et al., 2003; Casin et al., 2003; Antunes et al., 2005; Nogrady et al., 2005; Ribeiro et al., 2008; Mantilla et al. 2010; Souza et al., 2010; Tóth et al., 2010; Fierro-Amature et al., 2011; Temelli et al., 2012; Jugulete et al. 2013; Hassing et al., 2014).

RESULTS AND DISCUSSIONS

Therapeutic management of salmonellosis consist of pharmacotherapy, hygienic treatment and diet (Verdes, 1995; Perianu, 2003).

Pharmacotherapy

The aims of salmonellosis pharmacotherapy can be grouped into three basic categories:

(1) **Antibacterial Chemotherapy**: consist in

administration of antibiotics, chemotherapeutic agents or quinolones on the basis of antibiograms. In some circumstances, until the antibiograms result are available, broad-spectrum antibiotics active on Gram-negative bacteria can be used (Verdes, 1995). Groups of antibacterial drugs recommended in salmonellosis therapy were set out below:

Chloramphenicol (acts by inhibiting bacterial proteins synthesis) – is used in cases where infections are deemed to be life-threatening (humans and companion/exotic animals). It has very good absorption in the duodenum. According to studies conducted in Hungary, Barcelona, Mexico and India, antibiotic-resistance of *S. Typhimurium* to chloramphenicol increased due to a factor R acquired by several isolates (Ruiza et al., 1999; Nogrady et al., 2005; Crivineanu, 2009).

Beta-lactams (inhibit bacteria cell wall synthesis - the synthesis of peptidoglycan) – are usually used against gram-positive bacteria. Some beta-lactams are active against *Enterobacteriaceae* (mecillinam, amoxicillin, ampicillin), but are not currently recommended for treatment because bacteria can develop easily antibiotic-resistance by production of enzymes that break down the beta-lactam ring (Crivineanu, 2009). Other beta-lactams, like cephalosporins of third-generation (cefcape, cefdaloxime, cefditoren, cefetamet, cefixime, cefmenoxime, cefdinir, cefodizime, cefotaxime, cefteteram, cefpodoxime, cefovecin, cefpimizole, ceftamere, ceftibuten, ceftiolene, cefoperazone, ceftiofur, ceftizoxime, ceftriaxone, ceftazidime) and fourth-generation (cefclidine, cefepime, ceftuprenam, cefoselis, ceftazopran, ceftiprome, ceftquinome) have increased activity against gram-negative organisms (Crivineanu, 2009).

Sulfonamides (inhibit bacterial B vitamin folate synthesis - inhibit bacteria growing and reproduction) – are rarely used due to the development of bacterial resistance and hepatotoxicity (Antunes et al., 2004). To prevent developing of bacterial resistance, sulphonamides, usually sulfamethoxazole are commonly used in combination with trimethoprim under multiple brand names, including Septra, Bactrim, Cotrimoxazol,

Biseptol, and Sumetrolim (Stroescu 1989a; Verdes, 1995; Crivineanu, 2009; Perianu, 2003).

Tetracyclines (inhibit synthesis of proteins by bacteria, preventing growth) – are also used occasionally due to the emergence of drug resistant and lack of therapeutic response (Ribeiro et al., 2008). Also, recent studies reported that the antibiotic-resistance increased for the macrolides erythromycin and azithromycin that act in the same way like tetracyclines by inhibiting bacterial proteins synthesis (Temelli et al., 2012; Hassing et al., 2014).

Quinolones (interfere the replication and transcription of bacterial DNA) – are broad-spectrum antibiotics and one of the most commonly prescribed antibiotics in veterinary practice (Crivineanu, 2009). Quinolones, especially ciprofloxacin and enrofloxacin seem to be very effective in the treatment of salmonellosis (Tóth et al., 2010). Unfortunately, the excessive prescription of fluoroquinolone conducted to the development of bacteria resistance and the dose used in salmonellosis therapy gradually increased (Aarestrup and Wiuff, 2003).

Fosfomycin (inhibits bacterial cell wall biogenesis by inactivating the enzyme MurA) – is a broad-spectrum antibiotic, with useful activity against *Salmonella* spp. (Crivineanu, 2009).

Bacteriophage therapy (viruses that invade bacterial cells and disrupt bacterial metabolism causing lyse of bacteria) – use natural viruses of the gastrointestinal tract that destroy specific *Salmonella* isolates without affecting the commensals digestive bacteria. Over the time were performed multiple experiments on the effectiveness of treatment and therapeutic response with bacteriophages in salmonellosis during which were obtained both positive and negative results. According to researchers failures were due to anaerobic environment that may affect bacteriophages activity (Bielke et al., 2012).

Due to the increasing of *Salmonella* serotypes antibiotic-resistance, the options of therapy decreased progressively. In treatment options is necessary and essential to do antibiograms, based on appropriate antibiotic to be used (Perianu, 2003).

(2) **Symptomatic treatment:** consist in oral or/and parenteral administration of fluids and electrolytes. This is achieved by increasing the oral fluid intake (e.g., unsweetened teas, mineral still water, rice/carrot soups) and the administration of isotonic solutions [e.g., 0.9% sodium chloride (0.9% NaCl), lactated Ringer's solution, 5% dextrose in water (D5W), and Ringer's solution] subcutaneously or intravenously (drip) (Crivineanu, 2009; Perianu, 2003; Danes, 2011). Diarrhoea can be managed by oral administration of bismuth salicylate/bismuth subnitrate, decoction of rice, loperamide (slowing down the movements of the intestines by binding the opiate receptor in the gut wall, inhibiting the release of acetylcholine and prostaglandins) (Stroescu, 1989a), racecadotril (acetorphan; oral enkephalinase inhibitor used in the treatment of acute diarrhoea), diosmectite (Smecta or Smecdral; activated natural aluminosilicate clay consisting of a double aluminium and magnesium silicate, an anti-diarrheal absorbent natural clay used in acute gastroenteritis), and the bowel anti-inflammatory sulfasalazine, mesalazine or budesonide oral to reduce gut hypersensitivity and protect intestinal mucosa (Crivineanu, 2009).

(3) **Supportive therapy:** general tonics (caffeine, pentetrazole), glucose and vitamins (e.g., A, D3, C, E, K) (Verdes, 1995).

Client education

The environmental hygiene will be focused on specific microclimate conditions (optimum temperature), isolation of affected animals and periodical decontaminations of facilities. Temperature and air flow positively influence the reactivity of the organism to the action of the etiologic agent in the disease's progression and the efficacy of the treatment imposed.

It is recommended to provide along the state of *Salmonella* infection the following conditions: (1) hosing in shelter with the proper temperature, ventilation and humidity in accord with the season and animal condition; (2) isolation of infected animals, in order to limit the dissemination of pathogen; (3) removing of stress factors; (4) periodic environmental decontamination and cleaning. (Verdes, 1995; Perianu, 2003; Danes, 2011).

Diet

In the management plan of treating salmonellosis an essential place is held by diet due to its significant intervention in the disease's evolution with purposeful implication on animal organism by intestinal epithelial restoration, in healing period and in the constitution of the animal. Diet should be adapted to particularities of each clinical case. For instance is indicate the improving of feed rations by feeding stuffs with high nutritional value, vitamins and minerals, and carefully phosphorus content (Perianu, 2003).

CONCLUSIONS

Therapeutic management of *Salmonella* infections should be approached as a plan, following all goals and using the best antimicrobial therapy in order to control the risk of creating carrier animals. It is also recommended a continuous scientific research to discover the best antibacterial treatment and to exclude ineffective drugs against which *Salmonella* developed resistance.

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