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REVIEW ARTICLE

Salmonellosis in swine: Clinical perspectives

Minkyung Shim†, Sanghyun Hong†, Min-Jae Seok, Hyeun Bum Kim*

Department of Animal Resources Science, Dankook University, Cheonan 31116, Korea

*Corresponding author: hbkim@dankook.ac.kr

Abstract

Salmonella is one of the most important food-borne zoonotic pathogens, causing acute or chronic digestive diseases such as enteritis. The acute form of enteritis is common in young pigs of 2 - 4 months of age. The main symptoms include high fever (41 - 42℃), loss of appetite, and increased mortality within 2 - 4 days of onset of the disease. It is often the cause of increasing mortality, decreasing growth rate and reducing feed efficiency of piglets. In the case of chronic enteritis in pigs, the main symptom is weight loss due to the continuing severe diarrhea. *Salmonella enterica* serovar Typhimurium and *Salmonella enterica* serovar Choleraesuis are typical pig adapted serotypes, which cause one of four major syndromes: enteric fever, enterocolitis/diarrhea, bacteremia and chronic asymptomatic carriage. These syndromes cause a huge economic burden to swine industry by reducing production. Therefore, it is necessary that swine industries should strive to decrease Salmonellosis in pigs in order to reduce economic losses. There are several measures, such as vaccination to prevent salmonellosis, that are implemented differently from country to country. For the treatment of *Salmonella*, ongoing antibiotic treatment is needed. However constant doses of antibiotics can be a problem because of antibiotic resistance. Therefore, the focus should be made more on prevention than treatment. In this review, we addressed the basic information about *Salmonella*, route of infection, clinical symptoms, and prevention of Salmonellosis.

Keywords: prevention, productivity of the swine industry, *Salmonella*, Salmonellosis

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† Shim and Hong contributed equally to this work as the first authors.

Introduction

Salmonella is a non-lactose fermenting bacteria belonging to the family *Enterobacteriaceae*. *Salmonella* has fimbriae and peritrichous flagella, and it is a noncapsulated, gram-negative, short rod bacterium. Facultatively anaerobic *Salmonella* grows on defined media without special growth factors (Timoney et al., 1988). However, the quantification and isolation of *Salmonella* from feces is somewhat prone to failure since *Salmonella* is often less abundantly present among competitor bacterial species in feces. Multiple enrichments using specially formulated selective and differential media for the isolation of *Salmonella* have been devised in order to overcome this constraint. The two most useful of these are Xylose-Lysine-Deoxycholate (XLD) and xylose-lysine-tergitol (XLT) agars that have replaced MacConkey agar. In addition, the isolation of *Salmonella* in fecal contents using Rappaport-Vassiliadis R10 and tetrathionate broth has been effective. The optimum growth temperature for *Salmonella* is 37℃ (Timoney et al., 1988; Busse, 1995; Nye et al., 2002; Korsak et al., 2004).

It has been known that medically important salmonella may be considered as a single species, known as *Salmonella enterica*, which has more than 2,500 different serotypes (Murray et al., 1999). Clinically familiar names, such as *Salmonella typhimurium* or *Salmonella* serotype typhimurium*,* which would be renamed *Salmonella enterica* serotype Typhimurium are being used in most medical laboratories (Timoney et al., 1988; Hohmann, 2001).

Salmonella serovars commonly found in swine are a major human health problem in the world. The most common serotypes associated with human *Salmonella* infections include following 4 serotypes, *S enterica* serovar Typhimurium*, S.* Heidelberg*, S.* Agona*,* and *S.* Infantis (Foley and Nayak, 2008). As a common food borne diseases in humans, Salmonellosis is related to contaminated food, such as pork products that are an important source of *Salmonella* infection in humans. It has been shown that 9.6% of the pork in United States retail stores was contaminated with *Salmonella* (Duffy et al., 2000; Andino and Hanning, 2015).

The reduction of the opportunistic pathogens in the gastrointestinal tract of swine, including *Salmonella,* has been proposed as one of mechanisms for antibiotic-mediated growth promotion (AGPs). Nevertheless, it is not clear if the use of AGPs results in lower load or carriage of *Salmonella* (Dibner and Richards, 2005). If it is true, the reduction in opportunistic pathogens by AGPs is of importance in terms of accessing the mechanisms of growth promotion by AGPs as well as its relationship with public health.

Transmission, prevalence and clinical symptoms

Transmission

Transmission of *Salmonella* between pigs can occur through the fecal-oral and intranasal routes, involving colonization and dissemination of the gastrointestinal tract and organs such as lungs and tonsils. Also, airborne or direct nose-to-nose contact could increase the possibility of transmission of *Salmonella* in intensive pig production systems (Oliveira et al., 2007). In addition, several potential risk factors for *Salmonella* infection, such as poor management and hygiene have been identified (Table 1) (Wales et al., 2013). In general, all ages of pigs are susceptible to *Salmonella* infection, however, weaned and growing-finishing pigs are more prone to *Salmonella* infection (Meurens et al., 2009).

Prevalence

The prevalence of *Salmonella typhimurium* was higher (62.5%) than other *Salmonella* serovars, and the prevalence of *Salmonella* infection was 32.9% both in finishing pigs and weaned pigs in India (Kumar et al., 2014). Young pigs are more susceptible to Salmonellosis because of immature intestinal function, concurrent diseases, and changes of surrounding environment (Wales et al., 2013; Aiello et al., 2016). Of these reasons, it is advised that swine farmers should focus on both improved hygiene and husbandry of young piglets to prevent *Salmonella* infection.

Non-typhoidal *salmonella* (NTS) illness accounts for approximately one million cases in the United States alone (Scallan et al., 2011; Tamang et al., 2015). Moreover, *Salmonella* was the second most commonly reported zoonoses in the European Union and was the third most common reason of foodborne diseases in Korea. In Spain, García-Feliz et al. reported 43.1% of prevalence of *Salmonella* in finishing pig herds (Garcia-Feliz et al., 2007; Tadee et al., 2014). However, the prevalence of *Salmonella* was 5.58% in fattening pigs in Germany (Visscher et al., 2011; Tadee et al.,

Table 1. Potential risk factors for *Salmonella* infection (Wales et al., 2013).

Type	Possible Sources
Housing	Type of pen (slatted, push = through, straw yard)
Management	Number of staff Number of pigs on farm Time as a pig farm Age groups housed separately Feed source Sick pens Reintegration of recovered pigs Bedding source Bedding type Feeder/drinker systems
Biosecurity/hygiene	Staff contact with other pigs Visitors who have contact with other pigs Water supply (mains or borehole) Drainage Presence of wildlife species Proximity of waterways, scrubland, pig wastes, cattle wastes, or sewage treatment/landfill sites Feed storage (capacity and sealed/open bins) Presence of biosecurity measures (boot dips, well wash, and visitor/staff clothing) Pigs loaded at perimeter Site contained within perimeter fence Rodent controls Disinfectant: type and frequency

2014).

S. typhimurium is most commonly attributed to swine *Salmonellosis* in Europe. It becomes a source of contamination of pork products, and it causes tremendous economic and animal welfare costs (Arce et al., 2014). In the pig farms of the Tarai region of Uttarakhand, India, the most prevalent *Salmonella* serotype was *Salmonella* typhimurium that accounts for about 62.5% of known serotypes (Kumar et al., 2014).

S. Choleraesuis is especially adapted to pigs and is rarely detected in other species, however, it can also cause systemic infection in humans (Chang et al., 2013). *Salmonella* serovar Choleraesuis var. Kunzendorf was the main cause of *S.* Choleraesuis outbreaks in pigs in Europe (Pedersen et al., 2015). Nevertheless, *S.* Choleraesuis infection in humans is not frequent in Canada or United Kingdom (Barrell, 1987; Briggs and Fratamico, 1999; Onyango et al., 2014). Interestingly, it was the second most common cause of human Salmonellosis in Taiwan (Chen et al., 1999; Onyango et al., 2014).

Clinical symptoms

The main route of *Salmonella* infection in humans is ingestion of contaminated food products or direct contact. It makes livestock species a potential source of Salmonellosis (Zhao et al., 2006a; Clothier et al., 2010). In swine, *Salmonella* infections such as *S.* Choleraesuis or *S.* Typhimurium produce a variety of disease syndromes including septicemia, enteritis, and respiratory disease (Boyen et al., 2008; Foley et al., 2008; Huang et al., 2009; Vigo et al., 2009; Clothier et al., 2010). Piglets are especially vulnerable to *Salmonella* infection and this leads to high morbidity and mortality (Schierack et al., 2006; Wang et al., 2014).

Infections with *S.* Typhisuis and *S.* Choleraesuis usually result in swine typhoid, characterized by a severe systemic disease that may result in enteric and fatal systemic disease (Gray et al., 1996; Lichtensteiger and Vimr, 2003; Chiu et al., 2004; Chiu et al., 2005; Ku et al., 2005; Nishio et al., 2005; Zhao et al., 2006b; Boyen et al., 2008).

The main sign of *S.* Typhimurium, which is most commonly found in pigs, is usually diarrhea. However, *S.* Typhimurium infection in young pigs can cause significant disease such as increase of rectal temperature and occurrences of *S.* Typhimurium in the jejunum, cecum, tonsil, and mesenteric lymph node (Tanaka et al., 2010; Yin et al., 2014). Pigs can be asymptomatic with *S.* Typhimurium present in their tonsils, gut and gut-associated lymphoid tissues, and they can become *Salmonella* carriers (Berends et al., 1996; Verbrugghe et al., 2011). When pigs are infected with *S.* Typhimurium, they suffer from enterocolitis which is one of the clinical signs of *S.* Typhimurium infection. Those pigs can also become chronic carriers (Nollet et al., 2005; Gradassi et al., 2013).

S. Choleraesuis usually causes necrotizing enterocolitis, apart from septicemia, characterized by hepatitis, pneumonia, and cerebral vasculitis and also causes systemic infections in humans. (Reed et al., 1986; Wilkins and Roberts, 1988; Chang et al., 2013).

Prevention

Management

The efforts made to reduce Salmonellosis incidence differ geographically. In the EU, efforts are focused on the process from farm to processing. On the other hand, in the USA, interventions are applied at the processing level (Rajic et al., 2007; Wilhelm et al., 2012).

Despite of the different focuses to reduce Salmonellosis, the main prevention involves measures to improve good management practices and post-harvest hygiene on farms (Mousing et al., 1997; Alban et al., 2002; Schwarz et al., 2011). These days, the addition of organic acid to feed or water and the administration of probiotics or prebiotics to pigs have emerged as methods to control *Salmonella* in swine farms. It has been shown that these can decrease the faecal excretion of *Salmonella* as well (Casey et al., 2007; Creus et al., 2007; De Busser et al., 2009; Martin-Pelaez et al., 2010; Schwarz et al., 2011; Mejicanos et al., 2016).

Another way to reduce *Salmonella* infection in swine farms is all-in-all-out system. Based on this system, all pigs should enter and leave from the facility together at the same time and this should be applied in mating, farrowing, and nursery units. This system can help to reduce the risk of *Salmonella* infection since the pigs raised under the same management system are considered to have a similar disease status (Scott et al., 2006; Padungtod et al., 2008).

In addition, it has been proven that fermented feed, Lactobacillus casei-fermented feed, are good for pigs and reduce *Salmonella* infection. It has also been shown that it was effective in reducing pig diarrhea and intestinal burden of *Salmonella* as well (Yin et al., 2014). Giving feed fermented liquid to pigs was shown to improve the performance of pigs of all ages (Missotten et al., 2015).

It was suggested that the use of a mixed-bacterial-species competitive-exclusion culture can reduce both load and carriage of *Salmonella* (Genovese et al., 2003). Reductions in the fecal shedding of *Salmonella* resulted in diminished horizontal transmission between pen- and littermates (Genovese et al., 2003).

The use of antibiotics is not recommended because of Salmonella's intracellular persistence and antibiotic resistance. For this reason, vaccination may represent an attractive alternative for the reduction of *Salmonella* incidence in swine (Gradassi et al., 2013).

Vaccines

Even though, strict hygiene practices and rational husbandry resistance management are the best way to reduce the prevalence of *Salmonella*, this approach cannot be applied in countries where high prevalence of *Salmonella* infection is observed. In this case, vaccination is considered a major control measure to reduce *Salmonella* contamination at the early stages of meat production (Selke et al., 2007; Eddicks et al., 2009; Leyman et al., 2011; Xu et al., 2012; Pesciaroli et al., 2013).

Killed *Salmonella* vaccines have been used in pigs with variable results. This discrepancy between efficacy results of Killed *Salmonella* vaccines may be due to their poor ability to induce cell-mediated immunity in vaccinated pigs (Xu et al., 1993; Yamane et al., 2000; Davies and Breslin, 2003; Schwarz et al., 2011). On the other hand, attenuated live vaccine strains have been shown to offer better protection than Killed *Salmonella* vaccines (Haesebrouck et al., 2004). Live vaccine strains consist of strains that are attenuated, strains with a mutation in genes that are important for bacterial metabolism, or strains in which specific virulence genes are removed (Kramer et al., 1992; Lumsden and Wilkie, 1992; Mastroeni et al., 2001; Boyen et al., 2009; Schwarz et al., 2011).

Vaccination is one of the suggested methods to reduce the burden of *S.* Typhimurium on swine farms (Haesebrouck et al., 2004; Eddicks et al., 2009; Hotes et al., 2011; Pesciaroli et al., 2013) and it is one possible supplementary measure to reduce *Salmonella* infection. Nowadays, various vaccine studies have been conducted in pigs with various results (Roesler et al., 2004; Farzan and Friendship, 2010; Hotes et al., 2011; De Ridder et al., 2013a; De Ridder et al., 2013b). For example, SC54 vaccine, a *S.* Choleraesuis var. kunzendorf avirulent live strain, is effective to protect pigs against infection by virulent *S.* Choleraesuis and virulent *S.* Typhimurium (Kramer et al., 1992; Letellier et al., 2000).

Conclusion

Salmonella is a major concern to the swine industry because it leads to clinical illnesses in swine resulting in poor growth performance and profitability (Callaway et al., 2006). As such, *S.* Typhimurium infection in growing pigs causes growth retardation (Balaji et al., 2000; Turner et al., 2002a; Turner et al., 2002b). In the acute phase of the *Salmonella* infection, swines show a reduction of growth rate and develop a fever leading to lower profitability (Jenkins et al., 2004).

S. Typhimurium and *S.* Choleraesuis are typical pig-adapted serotypes. Infection by *Salmonella* results in economic losses in swine industries by causing serious clinical syndromes in weaned pigs. *Salmonella* infection in weaned pigs causes fever and continuous diarrhea. It is often the cause of increased mortality, decreased growth rate, and reduced feed efficiency. There are several measures, such as vaccination to prevent salmonellosis, that are implemented differently from country to country. For the treatment of *Salmonella*, ongoing antibiotic treatment is needed. However, constant doses of antibiotics can be a problem because of antibiotic resistance. Therefore, more focus should be made on prevention than treatment.

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