Study on the Synergistic Prevention of Control Effect of Genetically Engineered Vaccines and Drug Sensitivity - Guided Medication for Porcine Bacterial Diseases

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Abstract:Aiming at the limitations of traditional prevention of control measures for bacterial diseases in pig farms, this study explored the synergistic prevention of control effect of genetically engineered vaccines and drug-sensitive guided medication for bacterial diseases in pig farms. During the research, by analyzing the core principles and application status of genetically engineered vaccines and drug-sensitive guided medication, and combining experimental data to analyze their synergistic prevention of control effect, this study provides a scientific guidance scheme for the prevention of control of bacterial diseases in pig farms.

Keywords: Bacterial Diseases in Pig Farms; Genetically Engineered Vaccines; Drug-Sensitive Guided Medication; Synergistic Prevention of Control; Antibiotic Resistance

1. Introduction

In the current pig industry, traditional prevention of control measures for bacterial diseases in pig farms are limited by problems such as incomplete immune protection and increased drug resistance caused by the abuse of antibiotics, making it difficult to meet the needs of high-quality industrial development. However, the synergistic prevention of control model of genetically engineered vaccines and drug-sensitive guided medication can achieve the goal of "prevention first, combination of prevention and treatment": the former reduces the incidence rate of the herd through active immunity and decreases the base number of disease occurrence; the latter conducts precise treatment for sick individuals, reducing mortality and transmission risks. These two measures form a closed loop of prevention of control, which can significantly improve the overall prevention of control efficiency of bacterial diseases in pig farms. At the same time, it helps breeding enterprises reduce medication costs and breeding losses, and ensures the quality and safety of livestock and poultry products.

2. Core Principles and Application Status of Genetically Engineered Vaccines and Drug-Sensitive Guided Medication

2.1 Principles and Application Progress of Genetically Engineered Vaccines

2.1.1 Core Mechanism of Action

Centered on molecular biology techniques, genetically engineered vaccines modify or recombine pathogen genes to screen antigen components with strong immunogenicity but no pathogenicity. These antigens are delivered to pigs via vectors to induce specific immune responses (humoral immunity and cellular immunity) against infections. The mechanism involves three key links:

(1)Antigen screening and optimization: Gene sequencing is used to identify the boundaries between virulence and immunogenic genes, followed by the elimination of virulence genes and enhancement of immunogenic genes. Site-directed mutagenesis is applied to adjust the antigen structure or fuse it with adjuvant genes, thereby improving immunogenicity, accelerating antibody production, and increasing antibody titer.

(2) Vector delivery and antigen presentation: Viral, bacterial, or plasmid vectors are selected based on the physiological stage of the pig herd to carry antigen genes into pigs. After the antigens are released, they are processed by presenting cells, combined with MHC molecules, and presented to T cells. This activates T cell differentiation to promote cellular immunity and B cell differentiation for antibody production[1,2,3].

(3) Activation of immune effects: In humoral immunity, antibodies bind to pathogen

antigens to prevent pathogens from adhering to cells or activate complement to lyse pathogens. In cellular immunity, CD8+ T cells kill infected cells, while CD4+ T cells regulate immune responses to maintain stable immune effects.

2.1.2 Application Status and Existing Problems

In terms of application and promotion, the acceptance of genetically engineered vaccines in large-scale pig farms in China has gradually increased. Some pig farms with an annual output of over 10,000 pigs have applied them to prevent and control diseases such as *Streptococcus suis* disease and *Escherichia coli* disease. Among these, some pig farms have established a standardized procedure of "basic immunization + booster immunization". After application, the incidence rate of bacterial diseases in these farms is significantly lower than that in the traditional vaccine group, showing a remarkable immune effect.

However, three core problems remain in the application process:First, the matching degree between vaccines and local epidemic strains is insufficient. Pathogens in some regions have multiple sequence types, and universal vaccines have a low protection rate against some dominant sequence types, easily leading to immune failure.Second, immunization procedures are non-standard. To control costs, some medium-sized pig farms reduce the number of vaccine inoculations or delay the inoculation time, resulting in the antibody titer of the pig herd failing to reach the protective threshold and a decline in immune protection rate.Third, the awareness of grassroots pig farms is low. Among grassroots pig farms with an annual output of less than 1,000 pigs, most still rely on traditional inactivated vaccines, considering genetically engineered vaccines too costly while ignoring their long-term prevention of control benefits, which restricts the promotion scope[4,5,6].

2.2 Principles and Practical Status of Drug-Sensitive Guided Medication

2.2.1 Core Mechanism of Action

Based on the interaction among "pathogen-drug-host", drug-sensitive guided medication quantifies the sensitivity of pathogens to drugs through in vitro drug sensitivity tests and formulates precise medication schemes. Its core principles include three key points:

(1) Pathogen sensitivity detection: Pathogens are isolated from the diseased tissues of clinically sick pigs. After identification, the disk diffusion method (measuring the diameter of the inhibition zone to determine sensitivity) or the broth microdilution method (determining the minimum inhibitory concentration, MIC) is used to detect the sensitivity of pathogens to different drugs.

(2) Matching of drug action mechanisms: Appropriate drugs are selected based on the type of pathogen, infection site, and drug action mechanism. For example, drugs with strong tissue penetration are selected for respiratory infections, and drugs with strong mucosal adhesion are selected for intestinal infections. The combined use of drugs with the same mechanism is avoided to prevent the accumulation of drug resistance.

(3) Adaptation to host metabolic characteristics: The medication scheme is adjusted according to the age and physiological status of the pig herd. Piglets have low metabolic enzyme activity, so the drug dose needs to be reduced; pregnant sows need to avoid teratogenic drugs, and safe drugs should be selected with reduced administration frequency[7,8].

2.2.2 Practical Value and Application Effects

Drug-sensitive guided medication demonstrates three core values in pig farm practice:

(1) Reducing the occurrence of drug resistance: By accurately selecting sensitive drugs, the drug-resistant gene mutations caused by long-term use of a single drug are avoided, which can significantly reduce the drug resistance rate of pathogens to commonly used drugs and slow down the development of drug resistance.

(2) Lowering breeding costs: It avoids the waste caused by the use of drug-resistant drugs, reduces the risk of product discard due to drug residues, decreases the expenditure on antibacterial drugs, and improves the economic benefits of breeding[9,10].

(3) Improving treatment effects: It quickly screens effective drugs, shortens the disease treatment cycle, reduces pig herd mortality, and lowers the economic losses caused by epidemics.

3. Analysis of the Synergistic Prevention of Control Effect of Genetically Engineered

Vaccines and Drug-Sensitive Guided Medication

3.1 Selection and Basic Information of Experimental Pig Farms

Three large-scale pig farms (Farm A, Farm B, and Farm C) were selected, and key variables were controlled to ensure scientificity.

Pathogen verification: PCR sequencing confirmed that Farm A had *Streptococcus suis* (cps2J), Farm B had Actinobacillus pleuropneumoniae (APP, ApxII), and Farm C had *Streptococcus suis* (cps2J) + *Escherichia coli* (F4), eliminating the interference of virulence differences.

Consistent basic management: All farms used a corn-soybean meal diet (crude protein: 18%-20%). After weaning, the temperature for piglets was controlled at 24℃-26℃, and the humidity at 60%-65%.

Drug washout period: Antibiotics were discontinued 1 month before the experiment, and *Bacillus subtilis* was added to maintain intestinal health.

Table 1. Basic Information of Experimental Pig Farms

Pig Farm No.	Stock / Head (Sows / Piglets)	Breeding Model	Main Pathogens (Genotyping)	Annual Average Incidence Rate (%)	Routine Medications	Antibiotic History in the Past Month
A	500 / 3000	Intensive	*Streptococcus suis* Type 2 (cps2J$^+$)	18.2	Amoxicillin, Florfenicol	None
B	800 / 4800	Intensive	APP (ApxII$^+$)	25.6	Ceftiofur, Tilmicosin	None
C	600 / 3600	Semi-intensive	*Streptococcus suis* + *E. coli* (F4$^+$)	22.4	Enrofloxacin, Sulfonamides	None

3.2 Experimental Design and Grouping

3.2.1 Matching of Vaccines and Drugs

Farm A (*Streptococcus suis* Type 2): A recombinant subunit vaccine against *Streptococcus suis* Type 2 (containing CPS+MRP-EF antigens, adjuvant: Montanide ISA206) was used, with 2 mL/dose injected intramuscularly per piglet. For drug-sensitive medication, a preset detection panel including 8 antibiotics (penicillins, cephalosporins, macrolides) was used, targeting common sensitive drugs for *Streptococcus suis*.

Farm B (APP): A recombinant subunit vaccine against APP (containing ApxII+OmpA antigens) was used, with the same inoculation dose as Farm A. The drug-sensitive detection panel covered 6 drugs effective against respiratory pathogens, including florfenicol, ceftiofur, and tilmicosin.

Farm C (Mixed infection): A bivalent recombinant subunit vaccine against *Streptococcus suis* and *E. coli* (containing CPS+F4 antigens) was used, with 2 mL/dose. The drug-sensitive detection covered 10 antibiotics targeting both *Streptococcus suis* and *E. coli* to avoid missing pathogens in mixed infections due to single drug use.

3.2.2 Quality Control of Grouping

Random grouping: Stratified sampling was conducted according to piglet weight (5.5-6.0 kg, 6.0-6.5 kg, 6.5-7.0 kg) to ensure uniform body weight in each group ($P>0.05$).

Standardized operation: Inoculation was performed by the same team via cervical intramuscular injection (1.5 cm depth), and the dose error of drug-sensitive medication was <5%.

3.3 Data Collection and Monitoring Indicators

3.3.1 Data Control

Recording of morbidity: Two rounds of inspections were conducted at 9:00 a.m. and 5:00 p.m. daily to record the piglets' mental state (lethargy, irritability), body temperature (measured behind the ear, ≥40.5℃ was judged as fever), respiratory symptoms (cough, abdominal breathing), and diarrhea (fecal character score: 1 = formed, 2 = pasty, 3 = watery; ≥2 was judged as diarrhea). Accurate recording of morbid symptoms provided original data for calculating treatment efficiency.

Detection of immune indicators: Serum was collected via anterior vena cava (3 mL per piglet), and serum was separated by centrifugation and stored at -20℃. Indirect standard kits were used to detect antibody titer, strictly following the kit instructions. The OD450nm value was read automatically by a microplate reader to avoid manual interpretation errors, providing reliable data for dynamic analysis of antibody titer.

Monitoring of drug resistance: When isolating pathogens from sick pigs, samples were taken

from lung tissues (for respiratory symptoms) or feces (for diarrhea symptoms) and inoculated on corresponding media (*Streptococcus suis*: Columbia blood agar; APP: chocolate agar; *E. coli*: MacConkey agar). After culturing at 37℃ for 24-48 hours, pathogens were confirmed by biochemical identification, followed by drug sensitivity tests. The purity of isolated strains was ensured to be >95%, providing qualified strain samples for drug resistance rate analysis.

3.3.2 Indicator Correlation

Antibody titer and incidence rate, drug dosage and drug resistance rate, and growth performance and health indicators were monitored simultaneously to provide data support for effect analysis.

3.4 Analysis of Synergistic Prevention of Control Effects

3.4.1 Evaluation of the Immune Effect of Genetically Engineered Vaccines

3.4.1.1 Dynamic changes of antibody titer

Farm A: At 14 days after the first immunization, the average antibody titers of the synergistic prevention of control group and the single vaccine group were 1.220 and 1.205, respectively, with no significant difference, indicating similar initial immune responses of the vaccine under the two intervention models. At 14 days after the booster immunization, the titers of both groups increased to 1.850 and 1.820, still with no significant difference, indicating that booster immunization could effectively stimulate antibody production, which was related to the enhanced immunogenicity of the MRP-EF antigen in the vaccine. At 120 days after immunization, the titer of the synergistic prevention of control group remained at 1.380 (above the protective level), while that of the single vaccine group decreased to 1.145, showing a significant difference. This was because in the single vaccine group, some piglets had continuous consumption of the immune system due to bacterial infections (not controlled by precise medication), accelerating antibody consumption; in contrast, the synergistic prevention of control group quickly controlled infections through drug-sensitive medication, reducing antibody consumption and extending the protection period (see Figure 1).

Farm B: The change trend of antibody titer was consistent with that of Farm A. However, due to the stronger immunogenicity of the ApxII antigen, the average titer of both groups reached 1.920 after booster immunization, and the titer of the synergistic prevention of control group was 1.410 at 120 days after immunization, which was higher than that of Farm A. This further verified the influence of vaccine antigen type on immune effect.

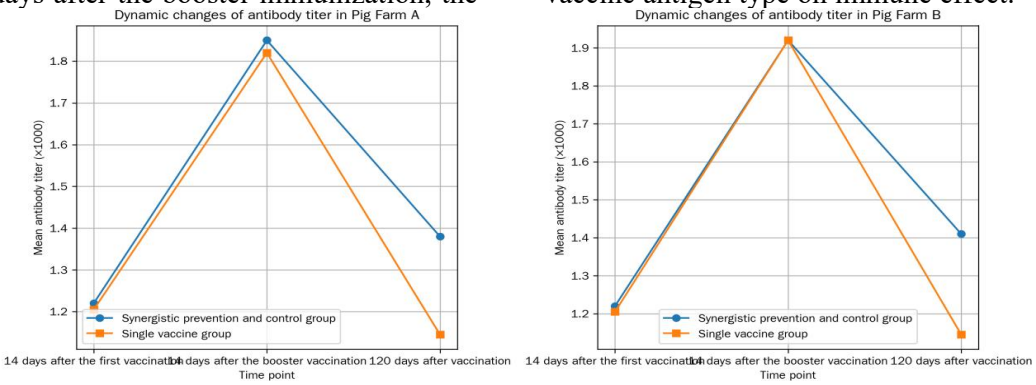

Figure 1. Dynamic Changes of Antibody Titer

Table 2. Immune Protection Rate of Each Group (%)

Pig Farm	Synergistic Prevention of Control Group	Single Vaccine Group	Difference
A	89.2	72.5	P<0.05
B	91.5	76.8	P<0.05
C	85.7	68.3	P<0.05

3.4.1.2 Immune protection rate

As shown in Table 2, the protection rate of the synergistic prevention of control group in all three pig farms was significantly higher than that of the single vaccine group, for the following reasons:

Farm B had a single pathogen (only APP), the vaccine antigens (ApxII+OmpA) were highly targeted, and drug-sensitive medication could quickly control APP infections, resulting in a more significant synergistic effect between the two measures.

Farm C had a mixed infection (*Streptococcus suis* + *E. coli*). Although a bivalent vaccine

was used, *E. coli* was affected by the intestinal flora, leading to weak intestinal mucosal immune responses in some piglets. In addition, controlling two types of bacteria simultaneously was required for mixed infections, increasing the difficulty of drug-sensitive medication, thus resulting in a slightly lower protection rate.

The single vaccine group had poor effects on drug-resistant strains due to empirical medication, failing to effectively control infections, which led to a decline in immune protection rate. This further proves the necessity of the synergy between "vaccine + drug-sensitive medication".

3.4.2 Analysis of the Therapeutic Effect of Drug-Sensitive Guided Medication

Farm B (APP infection): Drug sensitivity tests showed that APP was sensitive to ceftiofur and resistant to tilmicosin. Therefore, ceftiofur was used in the synergistic prevention of control group, while tilmicosin was used in the single vaccine group. After treatment, the treatment efficiency of feverish piglets in the synergistic prevention of control group within 48 hours was 94.3%, while that of the single vaccine group was 62.7% (see Figure 2). In terms of mortality rate, the synergistic prevention of control group had a mortality rate of only 3.2% (mostly piglets with severe infections), while the single vaccine group had a mortality rate of 15.6% (due to infection spread caused by ineffective drugs), showing an extremely significant difference ($P<0.01$). This fully verifies that "drug-sensitive medication based on MIC values" is more effective than empirical medication.

Farm C (Mixed infection): The synergistic prevention of control group used ceftiofur for *Streptococcus suis* and amikacin for *E. coli*. After combined medication, the treatment efficiency reached 89.2% with a mortality rate of 4.5%. The single vaccine group used enrofloxacin (empirical medication), but the drug resistance rates of *Streptococcus suis* and *E. coli* to enrofloxacin in this farm were 72% and 80%, respectively, resulting in a treatment efficiency of only 56.3% and a mortality rate of 18.2%. This further proves the importance of drug-sensitive guided medication for mixed infections.

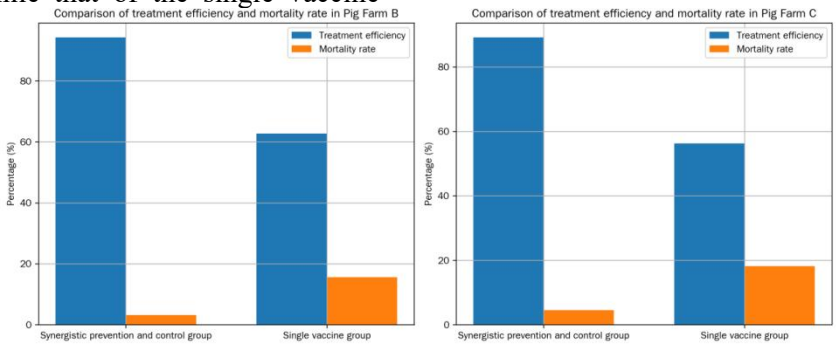

Figure 2. Treatment Efficiency and Mortality Rate

Table 3. Comparison of Core Indicators of the Three Groups

Indicator	Synergistic Prevention of Control Group	Single Vaccine Group	Blank Control Group
Incidence Rate (%)	8.6±2.3	21.4±3.5	38.7±4.2
Mortality Rate (%)	2.1±0.8	7.5±1.2	15.3±2.1
Average Daily Gain (g/d)	625±32	548±28	462±35
Feed Conversion Ratio	2.8:1±0.1	3.1:1±0.1	3.5:1±0.2

3.4.3 Comprehensive Effect Evaluation of Synergistic Prevention of Control

3.4.3.1 Health and growth performance

As shown in Table 3, the average daily gain of the synergistic prevention of control group was significantly higher than that of the single vaccine group and the blank control group, and its feed conversion ratio (2.8:1) was significantly lower than that of the latter two groups. The reasons are as follows:

The synergistic prevention of control group had a low incidence rate (8.6%), so piglets had low infection pressure, reduced energy consumption, and more nutrients were used for growth.

Although the single vaccine group was inoculated with vaccines, it still had an incidence rate of 21.4%. Infections led to a decrease in piglet feed intake (by approximately 15%-20%) and impaired

intestinal absorption function, resulting in an increased feed conversion ratio.

The blank control group had no vaccine protection, and an incidence rate of 38.7% caused growth retardation in a large number of piglets, resulting in the lowest average daily gain.

3.4.3.2 Economic and Ecological Benefits

Economic benefits: In addition to the direct benefits from improved growth performance, the synergistic prevention of control group reduced the number of dead piglets. At the same time, the reduced use of antibiotics lowered drug costs, further increasing profits.

•Ecological benefits: The reduced use of antibiotics in the synergistic prevention of control group decreased drug residues in pig farm sewage, reducing pollution to surrounding soil and water bodies. This is in line with the requirements of green breeding and the design concept of "integrating environmental management into the prevention of control system".

4. Conclusion

The analysis shows that genetically engineered vaccines can accurately target pathogens to build an immune barrier, while drug-sensitive guided medication achieves precise treatment through standardized tests. The synergy between the two forms a "prevention-treatment" dual guarantee, which can significantly reduce the incidence rate and mortality rate of bacterial diseases, reduce the risk of antibiotic abuse and drug resistance, and improve breeding benefits and food safety. Currently, synergistic prevention of control faces many challenges such as vaccine costs, technology popularization, and system integration, but new breakthroughs can be achieved through technological research and development, policy support, technology promotion, and management optimization. In the future, researchers should focus on the development of new vaccines and the innovation of drug-sensitive technologies, and further promote the upgrading of prevention of control of bacterial diseases in pig farms by building a regional prevention of control network, providing strong support for the healthy development of the pig industry.

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