Pharmacological improvement of metabolic processes in piglets in a state of postnatal physiological immaturity

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Abstract. The article presents results of the development of a method for improving metabolic processes in immature piglets. In order to achieve the purpose of the research, pharmacological preparations were selected taking into account the nature of changes in metabolic processes in piglets in a state of acquired immaturity. For this purpose, effects of riboflavin, Vicasol, potassium succinic acid and their combinations were determined separately. It was established that feeding immature piglets with acid potassium (0.125 g) combined with riboflavin (2.5 mg) and vicasol (0.3 g) for 18-21 days improves metabolic processes, ensures the growth and development of animals. Increased development of macroergs decreases the levels of lactic acid and fatty acids, restores semipermeable properties of cell membranes and mitochondria, improves the conjugation of respiration processes with oxidative phosphorylation. Metabolic processes become improved; values of the parameters reach those of mature animals. The method of improvement of metabolic processes in piglets in a state of postnatal immaturity is simple, does not require special equipment and technology. Its implementation removes 100% of the animals from the state of immaturity and increases their live weight by 42.8; the average daily gain is 33.1, the safety level is 39.7%.

1. Introduction
Postnatal immaturity of piglets is an acute problem. By the end of the lactation period, 17.36-33.33% of farm pigs and 18.30-29.40% of pigs bred by industrial enterprises have pronounced signs of acquired immaturity. The widespread immaturity affects productivity and safety of animals [1,2]. A number of Russian and foreign scientists are searching for the most effective ways to prevent immaturity.

Analysis of the main known methods allows us to conclude that they are rather laborious and require an individual approach. They do not correspond to the main link in the mechanism of changes occurring in the body of piglets in a state of immaturity. By their nature, they are stimulating and are aimed at activating metabolic processes, growth and development of animals; therefore, they are effective only at the initial stage of development of immaturity and ineffective in a state of full development of its symptoms.

The results of the studies by A. I. Kuznetsov [1-3] indicate that piglets in a state of immaturity have a special profile of metabolic processes. In the tissues and blood, they have an extremely low content of plastic and energetic substances, especially carbohydrates. Fats and proteins are predominantly used as an energetic material which accumulates the high acid content; as a result, structural and functional properties of membranes, including mitochondria, change, their energy activity and functionality of organs and systems decrease slowing the growth and development of the organism.
The research purpose is to develop a method for improving metabolic processes allowing for prevention of physiological immaturity of piglets.

2. Materials and research methods.
Analysis of Russian and foreign literature on bioenergy allowed us to take succinic acid potassium in combination with riboflavin and Vicasol for testing.

When preparing succinic acid potassium, succinic acid was used. Its therapeutic effect is due to the fact that it occupies one of the central places in the tricarboxylic acid cycle. Being a natural energy metabolite, it penetrates through membranes of cells and mitochondria that have the greatest need for energetic material, involving in redox processes and creating a kind of functional "push" for the formation and accumulation of ATP [4].

The combination with potassium can increase the therapeutic effect of succinic acid. Potassium is an intracellular and intramitochondrial element; it has a beneficial effect on the functions of mitochondria and redox processes [5].

The optimal and appropriate dose of succinic acid used for feeding piglets is 0.10-0.125 g/kg of live weight per day [6]. Higher doses are also effective, but not economical.

The use of riboflavin is based on the fact that it is part of flavin dehydrogenases (SDH, GPDH, monoamine oxidase) which are stressful enzymes that work intensively (and quickly wear out) under heavy loads on the body, especially in severe forms of pathology, including physiological immaturity. These enzymes are involved in the oxidation of succinic acid. Their formation and quantity are limited by the content of riboflavin in the body. Under normal feeding in pig farms and enterprises, the Riboflavin intake is not sufficient which causes the insufficient content and low activity of the above-mentioned enzymes. In this regard, it is reasonable to assume that the combined use of succinic acid, potassium and riboflavin will be accompanied by a positive effect. The daily need for riboflavin in piglets up to 10 kg of live weight is 2.0-2.5 mg [7].

Vicasol is used to form cells, in particular in mitochondria, an important peridin-nucleotide-menadione reductase enzyme that transfers hydrogen ions (H2 +) [7]. Vicasol can form new additional redox chains in critical moments which become a structural and functional basis for the released energy. Vicasol is similar in structure to ubiquinone and participates in tissue respiration and oxidative phosphorylation [8].

The daily dose recommended for young pigs is 0.08-0.3 g per head per day [8].

To determine the comparative effect of succinic acid potassium, riboflavin, vicasol and their combined use on the body of piglets in a state of postnatal immaturity, the following experiments were conducted. In a pig enterprise with 85 thousand pigs, in the Pig-Ballium sector, 5 groups of postnatally immature animals aged 26 days were formed: the first control group included 15 pigs, the second group included 15 pigs fed with vicasol (0.3 g per animal per day); the third group included 15 pigs fed with amber-acid potassium at a dose of 0.125 g per 1 kg of body weight; the fourth group included 15 pigs fed with riboflavin at a dose of 2.5 mg per head per day; the fifth group was fed with amber - potassium acid at a dose of 0.125 g per 1 kg of body weight, vicasol at a dose of 0.3 g per animal, and riboflavin at a dose of 2.5 mg per animal per day. All drugs were supplements to the basic diet. All animals were observed on the 26th, 44th and 47th days of life, while determining body weight, an absolute increase in body weight, the share of piglets with improved metabolic processes. The state of metabolism was investigated on the 47th day. As a control, a group of physiologically mature animals was used. Indicators of metabolism were studied by generally accepted methods. Animals with smaller body sizes and living weight (by 16-27.5%), weakened and disproportionate bodies, unsatisfactory fatness, with pale visible mucous membranes, dry, pale, grayish skin covered with thick tousled bristles, a body temperature within 40.1-40.70 C, a respiration rate of 40-44, a pulse of 139-145 times per minute were considered in a state of acquired immaturity. Animals with higher positive rates were physiologically mature.

3. Results and discussion
Table 1 shows that in the control group, the parameters were the lowest. On the 47th day of life, the body weight was 5.49 ± 0.13 kg, the absolute average daily gain was 8.9 g, and the safety level was 53.3%. 12.5% overcame the state of postnatal immaturity.

In the second group, by the end of the observations, the body weight was 6.01 ± 0.24 kg, the absolute average daily gain was 11.2 g, the safety level was 60.0%, of which only 22.2% were out of immaturity, which turned out to be higher than in the control group, respectively, by 9.5; 25.8; 6.7; 9.7%.

In the third group, by the end of the observation period, the body weight was 6.25 ± 0.16, the absolute increase was 12.8 g, safety was 66.6%; 30% of piglets overcame postnatal immaturity which is higher than in the control group by 13.8; 43.8; 13.3; 17.5%.

In the fourth group, under the influence of the drug, by the 47th day of life, the body weight was 6.80 ± 0.10 kg, the absolute average daily gain was 15.7. The safety level was 80.0%, 75% overcame immaturity. These figures exceeded the control ones by 23.8; 76.5; 26.7 and 62.5%.

Table 1. The effect of succinic acid potassium, vicasol and riboflavin on the growth and safety of piglets in a state of acquired immaturity

| Age, day | Group | Amount | Live weight, kg | Absolute gain, g | Safety, % | Exit from the immature state, % |
|----------|-------|--------|----------------|------------------|----------|-------------------------------|
| 26       | 1     | 15     | 3.63 ± 0.04    | -                | -        | -                             |
|          | 2     | 15     | 3.65 ± 0.08    | -                | -        | -                             |
|          | 3     | 15     | 3.57 ± 0.05    | -                | -        | -                             |
|          | 4     | 15     | 3.51 ± 0.09    | -                | -        | -                             |
|          | 5     | 15     | 3.47 ± 0.05    | -                | -        | -                             |
|          | 1     | 8      | 5.11 ± 0.09    | 8.2 ± 0.06       | 53.3     | 12.5                          |
|          | 2     | 9      | 5.81 ± 0.21    | 12.0 ± 0.27      | 60.0     | 22.2                          |
|          | 3     | 10     | 5.90 ± 0.17    | 12.9 ± 0.34      | 66.6     | 30.0                          |
|          | 4     | 12     | 6.20 ± 0.12    | 14.9 ± 0.26      | 88.0     | 58.3                          |
|          | 5     | 14     | 6.75 ± 0.27    | 18.2 ± 0.39      | 93.3     | 85.7                          |
|          | 1     | 8      | 5.49 ± 0.13    | 8.9 ± 0.31       | 53.3     | 12.5                          |
|          | 2     | 9      | 6.01 ± 0.24 *  | 11.2 ± 0.12 *    | 60.0     | 22.2                          |
|          | 3     | 10     | 6.25 ± 0.16 *  | 12.8 ± 0.08 *    | 66.6     | 30.0                          |
|          | 4     | 12     | 6.80 ± 0.10    | 15.7 ± 0.34      | 80.0     | 75.0                          |
|          | 5     | 14     | 7.84 ± 0.31    | 20.82 ± 0.26     | 93.3     | 100.0                         |

Hereinafter: * p <0.05; ** p <0.01; *** p <0.001

In the fifth group, by the end of the observation period, the highest efficacy of the drugs was observed. The body weight was 7.8 ± 0.31 kg, the absolute average daily gain was 20.8 g, the safety level was 93.0%; 100% overcame postnatal immaturity; the values were higher by 42.8; 133.1; 40.0 and 87.5% than those in the control group.

The state of metabolic processes in piglets under the influence of injected drugs is presented in Table 2. It can be seen that in the second group, the values of the parameters with the exception of the content of lactic acid and NEFA were lower in comparison with the values of similar indicators in mature piglets. They were as follows: dry substances - 70.0, total protein - 63.6, albumin - 151.7, globulins - 79.6, glucose - 48.2, glycogen - 44.8, total lipids - 45.3, total cholesterol - 35.2, lactic acid - 179.1, NEFA - 178.5, ATP - 70.3, ascorbic acid - 42.7, riboflavin - 53.3%. 

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In the fourth group, under the influence of the drug, by the 47th day of life, the body weight was 6.80 ± 0.10 kg, the absolute average daily gain was 15.7. The safety level was 80.0%, 75% overcame immaturity. These figures exceeded the control ones by 23.8; 76.5; 26.7 and 62.5%. 

Table 1. The effect of succinic acid potassium, vicasol and riboflavin on the growth and safety of piglets in a state of acquired immaturity
Table 2. Comparative characteristics of metabolic processes in immature piglets under the influence of succinic acid potassium, riboflavin and vicinal

| Indicator                        | Group (n = 10) | 1 - control | 2             | 3 | % to the 1st group | % to the 1st group |
|----------------------------------|---------------|-------------|---------------|---|-------------------|-------------------|
|                                  |               | X ± S x     | X ± S x       |   |                   |                   |
| Dry matter, %                    |               | 10.26 ± 1.20| 7.25 ± 0.15 **| 70.0 | 8.65 ± 0.23 *     | 84.3              |
| Total protein, g/l               |               | 78.64 ± 7.21| 50.01 ± 1.30 **| 63.6 | 59.80 ± 2.65 **   | 76.0              |
| Albumins, %                      |               | 28.36 ± 2.13| 43.01 ± 3.15 **| 151.7 | 40.17 ± 4.72 **   | 141.6             |
| Globulins, %                     |               | 71.64 ± 5.49| 56.99 ± 4.61 **| 79.6 | 59.83 ± 3.91 *    | 83.5              |
| Glucose, mmol/l                  |               | 5.96 ± 0.32 | 2.87 ± 0.13 ***| 151.7 | 40.17 ± 4.72 **   | 141.6             |
| Glycogen, mg%                    |               | 13.20 ± 1.18| 5.92 ± 0.49 ***| 151.7 | 40.17 ± 4.72 **   | 141.6             |
| Total lipids, g/l                |               | 4.02 ± 0.37 | 1.82 ± 0.36 ***| 151.7 | 40.17 ± 4.72 **   | 141.6             |
| Total cholesterol, mmol/l        |               | 4.92 ± 0.12 | 1.73 ± 0.04 ***| 151.7 | 40.17 ± 4.72 **   | 141.6             |
| Lactic acid, mmol/l              |               | 3.21 ± 0.09 | 5.75 ± 0.41 ***| 151.7 | 40.17 ± 4.72 **   | 141.6             |
| ATP, mg%                         |               | 2.12 ± 0.80 | 1.49 ± 0.08 ** | 151.7 | 40.17 ± 4.72 **   | 141.6             |
| NEFA, meq/l                      |               | 381.24 ± 29.60 | 680.60 ± 15.70 | 151.7 | 40.17 ± 4.72 **   | 141.6             |
| Ascorbic acid, mmol/l            |               | 64.90 ± 4.71| 27.70 ± 2.80 ***| 151.7 | 40.17 ± 4.72 **   | 141.6             |
| Riboflavin, µg%                  |               | 31.70 ± 3.21| 16.90 ± 2.14 ***| 151.7 | 40.17 ± 4.72 **   | 141.6             |

**Note:** * - P≤0.05; ** - P≤0.01; *** - P≤0.001

In the third group, the content of the substances, with the exception of albumin, lactic acid and NEFA, was higher than in the second one: dry substances - by 19.3, total protein – by 9.79, globulins – by 2.84,
glucose – by 7.3, glycogen – by 20.3, total lipids – by 12.8, total cholesterol – by 22.0, ATP – by 10.7, ascorbic acid – by 17.0, riboflavin – by 35.4; the content of albumin was lower by 6.7, lactic acid – by 18.1, NEFA – by 11.7%. At the same time, the level of concentration of most of these substances remained lower than that in mature piglets, and amounted to the value of similar parameters: dry matter - 84.3, total protein - 76.0, globulin - 83.5, glucose - 51.7, glycogen - 53.9, total lipids - 50.7, total cholesterol - 42.9, ATP - 77.8, ascorbic acid - 49.9%. The content of albumin, lactic acid and NEFA was higher by 41.6; 46.7; 57.6%, respectively.

In the fourth group, most of the parameters were significantly higher than in the second group: dry substances - by 22.8, total protein - 28.6, globulins - 21.7, glucose - 77.7, glycogen - 93.6, total lipids - 27.5, total cholesterol - 36.4, ATP - 22.1, ascorbic acid - 44.9, riboflavin - 57.4, albumin content is lower by 28.8, lactic acid - 36.7, NELC - 27.9%.

However, in comparison with similar parameters in mature piglets, they were lower: dry substances - 86.7, total protein - 81.8, globulins - 96.8, glucose - 85.6, glycogen - 86.4, total lipide - 57.7, total cholesterol - 48.0, ATP - 85.8, ascorbic acid - 61.9, riboflavin - 83.9%, the values of albumin, lactic acid and NEFA are higher, respectively, 8, 0; 13.4; 28.6%.

In the fifth group, the values of the parameters were closer to those in the mature animals: dry substances - 98.0, total protein - 95.5, albumin - 94.4, globulins - 102.2, glucose - 96 , 3, glycogen - 96.5, total lipids - 96.8, total cholesterol - 95.7, lactic acid - 104.0, NEFA - 103.2, ATP - 97.2, ascorbic acid - 93.2, riboflavin - 100.6%.

The results are due to the fact that amber-acid potassium, riboflavin and vicasol, being natural metabolites, easily penetrate through the membranes of cells and mitochondria in the tissues of organs that have the greatest need for energy materials, involve in recovery processes that ensure the release of energy and its accumulation in macroergic compounds. The increased formation of macroergs causes a gradual decrease in the content of lactic acid and fatty acids (21, 391), restoration of semi-permeable properties of cell membranes and cell orga, in particular mitochondria, normalization of the conjugation of respiration processes with oxidative phosphorylation. Restoration of the synthesis of high-energy compounds contributes to the involvement of energetic substances into the tricarboxylic acid cycle which is the main condition for maintaining basic vital processes, growth and development of animals.

4. Conclusion
Feeding piglets in a state of postnatal immaturity with succinic acid potassium (0.125 g/kg per live weight) in combination with riboflavin (2.5 mg and vicasol at a dose of 0.3 g per head per day) improves metabolic processes, growth and development of piglets. The use of drugs prevents postnatal immaturity, increases the live weight of animals by 42.8%, and safety – by 39.7% keeping it at the level of 93.0%.

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