EVALUATION OF THE EFFICACY OF IRON POLYMALTOSE COMPLEX IN THE PREVENTION OF ANAEMIA IN PIGLETS

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Abstract

The aim of this study was to evaluate the efficacy of oral application of iron polymaltose complex (IPC) in the prevention of iron deficiency in piglets. The piglets in group I (n = 15) were treated with iron dextran (200 mg of Fe³⁺, i.m.) at the age of 3 d. In group II (n = 19), the piglets were given 100 mg of Fe³⁺ as IPC orally at the age of 3 and 11 d. The piglets in group III (n = 19) received oral application of 100 mg of Fe²⁺ as ferrous fumarate at the age of 3 and 11 d. The piglets in group IV (n = 12) served as an iron deficient control group. The haemoglobin concentration and iron concentration in blood plasma in IPC treated group were comparable to the ferrous fumarate group. It is concluded that the IPC showed a comparable efficacy of IPC in the anaemia prevention as ferrous fumarate.

Key words: piglets, anaemia, ferrous fumarate, iron polymaltose complex.

Iron deficiency is a very common disorder seen in swine production. The piglets are born with limited reserves of iron (50 mg) (25) and without additional iron supplementation; they develop anaemia within 10-14 d after birth (5). The most common method of iron treatment is an injection of 200 mg of Fe³⁺ in the form of iron dextran to 3-day-old piglets (26). An alternative to the iron injection is an oral application of iron salts. Iron fumarate (15, 21) and iron lactate (15, 22) have been used in pig production. Only iron salts with bivalent iron (Fe²⁺) should be used in oral preparations since according to Dieztfelbinger (4) the bivalent iron is up to 16 times better absorbed than Fe³⁺. In human patients, the use of ferrous salts is limited by their possible adverse effects, such as gastric intolerance, nausea, vomiting, constipation, and diarrhoea (10). Iron polymaltose complex (IPC) is a novel compound with potential use for anaemia prevention. It binds iron in its ferric form (Fe³⁺) and has a very good safety (7, 8). However, its efficacy in the treatment of anaemia remains controversial. To our knowledge, IPC has not yet been tested for anaemia prevention in piglets. Therefore, we decided to undertake the following study.

Material and Methods

Experimental design. The piglets were divided into 4 groups (split litters): two experimental groups and two control groups. Group I (positive control group, n=15) was injected i.m. with 200 mg of Fe³⁺ in the form of iron dextran on day 3 of the piglets’ life. Group II (iron polymaltose group, n=19) was given 100 mg of Fe³⁺ orally as iron polymaltose complex (IPC) on day 3 of the piglets’ life. The same dose was repeated at the age of 11 d. Group III (ferrous fumarate group, n=19) was given orally 100 mg of Fe²⁺ as ferrous fumarate on day 3 of the piglets’ age. The same dose was repeated on day 11. Group IV (negative control group, n=12) was not given any iron preparation until piglet age of 17 d. At this age, the piglets were injected i.m. with 200 mg of Fe³⁺ in the form of iron dextran.

From day 7 of age all the piglets had an access to creep feed (SKS weaning pellets, Slavkovské krmné směsi a.s., iron content 220 mg/kg). The piglets were weaned at the age of 27 d.

Sampling and analyses. Blood was collected from the vena cava cranialis. EDTA (ethylenediaminetetraacetic acid) was used as anticoagulant for the haematological examination. Heparin was used as anticoagulant for the determination of iron concentration in blood plasma. The blood was taken and the piglets were weighed on days 3, 11, 17, 25, and 31.

The following haematological indices were measured using an automatic analyser Sysmex EX-2100: haemoglobin (Hb) concentration, packed cell volume (PCV), red blood cell count (RBC), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), reticulocyte count (RET), percentage of reticulocytes (RET, %), haemoglobin concentration in reticulocyte (RET-He), and index RET-Y. The index RET-Y provides a relative measure of the equivalent of a mean corpuscular volume of reticulocytes.
Iron (Fe) concentration in blood plasma was determined photometrically by measuring iron complex with ferrozine (Iron liquid 917, Roche Diagnostic, Germany).

The differences between groups were evaluated by non-parametric Kruskal-Wallis ANOVA test at the level of significance P<0.05. The changes within groups were evaluated by non-parametric Friedman ANOVA and subsequently by a paired Wilcoxon test at the level of significance P<0.01. The haematological indices are presented in Figs 1-10. The iron concentration in blood plasma and body weights are presented in Tables 1 and 2.

Results

The haematological indices and iron concentration in blood plasma in IPC group (group II) were comparable to ferrous fumarate group (group III). The examined indices of groups II and III showed similar manner of the development, i.e. Hb, PCV, MCV, and MCH reached their maximal levels at the age of 17 d and then declined.

In iron dextran group (group I), at the age of 31 d, the indices of Hb, PCV, RBC, RET-Y, and Fe were found to be significantly higher compared to group III. With exception of RET-He and RET-Y on day 11, the examined indices of group II did not differ significantly from those in iron dextran group.

At the age of 11 d, the indices of RET-He and RET-Y of iron dextran group were significantly higher than those in orally treated groups. Reticulocyte indices RET-He and RET-Y of groups I and III reached their maximal levels at the age of 11 d and showed a decline thereafter. Reticulocyte indices of RET and RET % of groups I, II, and III reached maximal levels on day 11 of life and then declined.

In group IV, the indices of Hb, PCV, RBC, MCV, MCH, RET, RET %, RET-He, RET-Y, and Fe started to be significantly lower than those in the other groups as early as from 11 d of age. One week after iron application (i.e. on day 25) the indices of Hb, PCV, MCV, MCH, RET, RET%, and Fe increased significantly.

At the age of 17 d, the body weight in group IV started to be significantly lower compared to groups I, II, and III.

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<td>Iron concentration in blood plasma (mean ± SD, µmol/L)</td>
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Letters <sup>a</sup>, <sup>b</sup>, <sup>c</sup> express significant differences between the groups at the level of significance P<0.05

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<td>Body weight during the trial (mean ± SD, kg)</td>
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<td>Days of age</td>
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Letters <sup>a</sup>, <sup>b</sup>, <sup>c</sup> express significant differences between the groups at the level of significance P<0.05
Fig. 1. Hb concentration.

Fig. 2. PCV volume.

Fig. 3. RBC count.

Fig. 4. MCV.

Fig. 5. MCH.

Fig. 6. MCHC.

Fig. 7. Reticulocyte count.

Fig. 8. Percentage of reticulocytes.
Discussion

Iron polymaltose complex is a novel compound, which binds iron in its ferric form and follows iron absorption, very dissimilar to that of ferrous iron salts. The main pathway for Fe$^{2+}$ absorption is a passive diffusion through duodenal enterocytes and therefore, with higher dose, iron intoxication may occur (8). On the contrary, IPC is practically non-toxic, since iron is released from the complex gradually and is absorbed by active transport with rate determining competitive ligand exchange (8). Moreover, IPC is a non-ionic complex, which does not release any free radicals. It is thus deprived of all toxic effects found due to the release of free radicals in the ionised iron salts (24).

The active transport is energetically dependent. Iron is therefore maximally absorbed when administered with or after meals (8, 13, 18). Food components such as phytic acid, tannin, soy bean flour, oxalic acid, sodium alginate, and tetracyclines in the gastrointestinal tract may react with iron (II) or iron (III) salts giving rise to non-absorbable iron complexes and thus decreasing the concentration of bio-available iron (8, 9). Since there is no interference between IPC and feed components, the bioavailability is not negatively influenced.

The bioavailability and efficacy of IPC has been evaluated by several authors with variable results. Several studies in human medicine have demonstrated high efficacy and safety of IPC in the treatment of anaemia (1, 6, 20). For instance, in blood donors, side effects were less frequent with IPC when compared with ferrous sulphate (11). According to Jacobs (12), the iron absorption from ferrous salts and IPC is quantitatively equivalent, in both experimental animals and human subjects. Reddy et al. (19) found that in terms of efficacy (higher Hb), IPC was superior to ferrous fumarate in the treatment of iron deficiency anaemia.

In our study, we have found a comparable efficacy of IPC in the anaemia prevention with ferrous fumarate. Our results are in agreement with Sas et al. (21) and Borbolla et al. (3). Sas et al. (23) stated that ferrous salts and IPC have comparable effects in the treatment of iron deficiency anaemia. Borbolla et al. (3) found the same efficacy of IPC in the treatment of anaemia in newborn children as that of iron sulphate.

In contrast to these studies, Malhotra et al. (16) found that ferrous sulphate showed significantly higher bioavailability as compared with IPC. Additionally, Arvas and Gür (2) reported that IPC was not as effective as ferrous sulphate, although it increased haemoglobin and serum iron. Mehta (17) reported failure of IPC in correction of iron deficiency anaemia in pregnant women.

In our study, we have found that, at the age of 25 and 31 d, haemoglobin concentration and iron concentration in blood plasma in the ferrous fumarate group was lower compared to iron dextran group. The iron concentration of IPC group was also lower at the age of 25 and 31 d than that in iron dextran group. Therefore, higher doses of iron in both orally treated groups should be recommended to achieve an efficacy comparable to intramuscular administration of iron dextran.

It is concluded that, under conditions of our trial, the efficacy of oral administration of IPC in anaemia prevention in piglets was comparable with that of oral administration of iron fumarate.

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Reference

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