DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

Iron is an essential microelement for biological processes since it participates in multiple enzymatic reactions as a part of iron-sulfur clusters, heme prosthetic groups and other iron-containing centers, which makes it indispensable for almost all living organisms. On the other hand, this metal may generate through the Fenton chemistry, a powerful oxidant - hydroxyl radical (˙OH) and thus may be responsible for DNA damage, lipid peroxidation and protein modification. Taken together, redox properties of iron makes this metal essential in biology but potentially toxic, especially in an oxygen environment. According to WHO, in humans, anemia is the third worldwide health disorder, while Iron Deficiency Anemia (IDA) dominates among other anemia. The main cause of IDA are insufficient dietary intake and duodenal absorption of iron, or iron loss from bleeding. Iron deficiency causes approximately 30% of all anemia cases worldwide, and mostly affects preterm children and premenopausal women. IDA affects nearly 1 billion people all over the world. In 2013 anemia due to iron deficiency resulted in about 183,000 deaths – down from 213,000 deaths in 1990. The results of several studies, including our own, indicate that newborn piglets are a suitable model, with which to explore iron metabolism in the neonatal period. First, iron deficiency anemia IDA is the most prevalent deficiency disorder during the early postnatal period in pigs, and frequently develops into a critical illness. It seems that the pig model of IDA accurately reflects this defect observed in pre-term human neonates as the iron content in their liver is very low. Intramuscular administration of large amounts of iron dextran (FeDex) on days 3-6 postpartum is a current practice in the swine industry, and has been proven to rectify the hematological status of piglets. However, it seems unlikely that 100-200 mg of iron (a commonly applied dose) given in a single injection to a piglet with only about 40-50 mg of iron in its body at birth, is efficiently metabolized and detoxified. Moreover, high parenteral intake of supplemental iron may easily perturb the tight control of systemic iron metabolic processes. In this context, iron supplementation in piglets raises the question of the role of hepcidin (Hepc), the most important hepatic hormone responsible for inhibition of duodenal iron absorption and iron reutilization in reticuloendothelial system (RES). With the development of nanotechnology, nanoparticles have shown application prospects since 1970s. Iron nanoparticles (INPs) have become a powerful tool for several applications acting as a potential drug or gene carrier. However, little is known about the usefulness of INPs in the treatment/prevention of iron deficiency anemia. Based on available data showing high INPs bioavailability, lack of their accumulation and toxicity in tissues and finally considering the evidence of their capacity to cross biological membrane, we decided to use of IONPs (Iron Oxide Nanoparticles) for the treatment of IDA in young pigs. Importantly, last conference of the European Iron Club in Innsbruck in 2016 was largely dedicated to iron nanoparticles and liposomial iron (LI) and several communications clearly indicated the possibility of using nanoparticles of Fe (II/III) as a safe and well absorbed oral iron supplement. Likewise, the results of our pilot study on liposomal iron have raised a lot of interest at the 7th Congress of the International BioIron Society in Los Angeles, USA, May 7-11, 2017.There is no evidence so far, that IONPs are used for iron supplementation in piglets. In most mammals there is no natural regulated pathway for the removal of iron excess from the organism. Therefore, the absorption of iron by duodenal enterocytes must be very tightly controlled. During last 20 years a number of transmembrane proteins implicated in the intracellular transport of both non-heme and heme iron as well as iron export to the extracellular environment have been identified. However, in terms of IONPs absorption, the role of duodenal iron transporters haven't been considered yet. Anemic pig neonates seem to be an ideal animal model for exploring molecular mechanisms of IONPs absorption and utilization as well as for designing new strategies of iron supplementation. In the frame of our project, we propose the experiment using Polish Landrace piglets receiving daily *per os* from day 5 after birth various iron nanoparticle or LI preparations suspended in 2 ml of the milk replacer. The main goal of our study is to identify duodenal and hepatic pathways involved in the absorption and metabolism of IONPs and/or IONPs-derived iron as well as underlying molecular mechanisms. In this purpose we will use genomics and proteomics approaches. Our project should also clarify the question of potential toxicity of IONPs.

To sum up, we plan for the first time to verify the usefulness of IONPs given to piglets *per os* for preventing/treating iron deficiency anemia in neonatal period. We expect to provide evidence showing that oral IONPs or LI supplementation of piglets is at least as efficient in treating neonatal iron deficiency as routine parenteral supplementation with iron dextran, which is largely practiced in swine industry.