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DISORDER OF IRON METABOLISM IN HYPOXIC PULMONARY HYPERTENSION RATS

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¹Ying Li, ²Xiao-Hui Li, ¹Guo-Ping Yang, ¹Zhi-Jun Huang, ¹Hong Yuan. ¹Center of Clinical Pharmacology, Third Xiangya Hospital, Central South University; ²Department of Pharmacology, School of Pharmaceutical Sciences, Central South University

Objectives Iron supplement is efficient to inhibit the increase of pulmonary arterial systolic pressure (PASP) induced by hypoxia. And recently, iron deficiency is normally observed in idiopathic pulmonary arterial hypertension (IPAH) patients, while the situation of iron metabolism and its regulatory mechanism under hypoxic pulmonary hypertension (HPH) is seldom known.

Methods 4-weeks hypoxia induced hypoxic pulmonary hypertension (HPH) in 4 rats. Beside blood regular test, blood samples were collected for determination of several factors related to iron metabolism including iron, ferritin, transferrin and hepcidin, which is synthesised in liver and plays a key role in inhibiting iron absorption, release and storage. Furthermore, RNA and protein were extracted from liver tissues to evaluate the transcriptional level of hepcidin and protein expression of the upstream regulator of hepcidin, BMP6.

Results WBC ($5.78 \pm 2.86 \times 10^9/l$ vs $1.60 \pm 0.59 \times 10^9/l$) and MCV (61.28 ± 2.01 fl vs 57.58 ± 2.39 fl) were decreased in HPH rats showed from blood regular test, while RBC, Plt did not change compared with control group. Iron concentration was significantly decreased in HPH rats (12.1 ± 3.43 ng/ml and 8.6 ± 1.30 ng/ml in control rats and HPH rats respectively), while the plasma level of transferrin (0.67 ± 0.13 nmol/l vs 1.02 ± 0.23 nmol/l) and hepcidin (5.87 ± 0.50 ng/ml vs 7.72 ± 0.75 ng/ml) were increased. Plasma level of ferritin was also decreased but the change is not significant (25.7 ± 4.71 ng/ml vs 19.7 ± 3.55 ng/ml, $p=0.052$). Q-PCR and western blot experiments showed that hepcidin mRNA level and BMP6 protein level were both significantly increased in liver.

Conclusions Dysfunction of iron metabolism in HPH rats was observed and an up-regulated BMP6/hepcidin signalling pathway in liver may contribute to this progress. BMP/SMAD-hepcidin signalling may play a critical role to regulate iron metabolism in HPH and iron supplement may be a potential treatment for HPH patients