Abstract

Present work has been focused on the importance of the products of the heme catabolic pathway, in particular under conditions of unconjugated hyperbilirubinemias (neonatal jaundice and Crigler-Najjar syndrome (CNS)). The second part of the project was focused on the improvement of some pharmacological approaches used in the treatment of these diseases, as well as on studies of bilirubin products that are formed during the treatment by phototherapy (PT).

Neonatal jaundice is one of the most common complications in neonates. Currently, there is no efficient pharmacotherapy and the treatment with blue light is used as a gold standard for severe neonatal jaundice. However, the absolute safety of PT has still not been confirmed. In this context, it is important to note that some neonatologists start the PT before serum bilirubin levels reach the recommended values and that patients with CNS type I (CNSI) are forced to be on life-long PT (unless undergoing liver transplantation).

The focus of the present project was to study biological effects of bilirubin photoisomers (PI) in an *in vitro* model of the human neuroblastoma SH-SY5Y cells that are used for studies of the neuronal metabolism. In further studies performed on animal model of hyperbilirubinemic rats and mice, we investigated a suitable gene therapy to be used in CNSI patients with the aim to reduce or eliminate the need of PT. Finally, we have compared the efficacy of PT, exchange transfusion (ET) and human serum albumin administration (HSA) in the therapy of CNSI and severe neonatal jaundice with respect to determination of free bilirubin (Bf) levels and bilirubin concentrations in various brain tissue compartments in the hyperbilirubinemic Gunn rats.

Key words: Haem metabolism, bilirubin, neonatal jaundice, Crigler-Najjar syndrome, phototherapy, bilirubin photoisomers, bilirubin oxidation products.