What is Important about the Effect of Clofibrate on Neonatal Hyperbilirubinemia?

Mohammad Torkaman[1] and Amin Saburi[2]

[1] *Department of Pediatric, School of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran*

[2] *Health Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran*

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Dear Editor

We read with interest the manuscript by Habibi *et al.* entitled *"The Effect of Clofibrate on Hyperbilirubinemia of Term Neonates"* (1). They skillfully reported an interesting investigation about the efficacy of clofibrate on the neonatal jaundice. They successfully used single dose of clofibrate (100 mg/kg) along with intense phototherapy in full term infants to treat unconjugated hyperbilirubinemia in comparison with intense phototherapy alone in control group. It seems that there are some remarks which must be considered before generalizing the results.

The lipid lowering effects of Clofibrate were identified well. Clofibrate is one of fibrates which activates peroxisome proliferator-activated receptors (PPARs) and modulates plasma lipid specially very-low density lipoproteins. Lipid and unconjugated bilirubin can conjoint together and also can bind to the serum transporters such as albumin (2,3). Therefore, change in bilirubin amounts (total or indirect) must be adjusted with regarding to the lipid profile alteration to estimate the true changes in amount of bilirubin. Also, the pediatric and maternal nutrition can affect serum lipid profile and liver enzyme activity as well as bilirubin level (4). Therefore the cases must be matched for nutrition with the control group. On the other hand, lipids are one of the most important substrate which is necessary for cell growth and development especially in infancy therefore the long term use of clofibrate can impair organ development and growth.

The authors have used 100 mg/kg dose of Clofibrate although the previous report was confirmed the efficacy of 50 mg/kg (5) of the neonatal jaundice whereas the cytotoxic effects of clofibrate on different types of cells (especially hepatocyte and myocyte), with particular reference to cancer induction and progression, are a challenging issue yet. Several intra and extra cellular processes including mitochondrial and peroxisomal fatty acid uptake and beta-oxidation, intracellular lipid trafficking, inflammation, cell proliferation and death are modulated by PPAR ligands such as clofibrate. However, recent studies have been confirmed the proapoptotic, antiproliferative, and differentiation-promoting activities of clofibrate (6). Therefore, it seems necessary to measure liver function tests and observe other side effects after using clofibrate particularly after frequent prescription.

Effects of fibrats on red blood cell (RBC) conformation (directly on RBC membrane or indirectly on lipid regulation and also RBC membrane) and in this way on bilirubin production in neonatal hyperbilirubinemia were reported previously (7,8). The serum half-life of single dose of clofibrate can reach up to more than hundred hours therefore it is suggest measuring the long-term effect of clofibrate although the authors were evaluated 48 h after treatment. The pure efficacy of clofibrate regardless of phototherapy must be evaluated in further investigations to confirm its efficacy and implementing in daily practice. It seems that clofibrate faces several serious queries to implement for daily practice.

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Corresponding Author: Amin Saburi
M.D. & Researcher, Health Research Center, Baqiyatallah University of Medical Sciences, Mollasadra St, Vanak Sq, Tehran, Iran
Tel: +98 21 88600062, 912 7376851, Fax: +98 21 88600062, E-mail: aminsaburi@yahoo.com

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