DOI: 10.4103/0971-5916.215565

Quick Response Code:

XXIII international bile acid meeting: Bile acids as signal integrators and metabolic modulators, D. Häussinger, U. Beuers, V. Keitel, M. Trauner, editors (Karger, Basel, Switzerland) 2015. 158 pages. Price: Not mentioned

ISBN 978-3-318-05436-1

This report presents the proceedings of Falk symposium 194 held in Freiburg, Germany in October 2014. One may rate the top two advances in the field of bile acids covered in this book as the introduction of farnesoid receptor agonists (obeticholic acid) to treat non-alcoholic fatty liver disease (NAFLD) and the discovery of a bile acid transporter as a critical receptor for entry of hepatitis B and D viruses into the hepatocyte.

We currently lack effective drugs to treat NAFLD. Bile acids modulate insulin signalling and improve insulin resistance in cell-based and animal studies. Farnesoid receptor activation inhibits hepatic gluconeogenesis and hepatic glucose output; and reduces lipogenesis and very low density lipoprotein formation. Farnesoid receptor agonists also have anti-inflammatory and anti-fibrotic properties. Bile acid derivative INT-747, a potent activator of farnesoid receptor, reduces liver fat and fibrosis in animal models. Farnesoid receptor agonists (like INT-747) have been shown to improve insulin resistance and NAFLD in humans. The symposium proceedings mention that the results of the FLINT trial, to see if INT-747 improves histology of NAFLD are awaited. These results were subsequently published, reporting that INT-747 (also known as obeticholic acid) improves the histology of NAFLD in humans. However, 23 per cent of the patients on obeticholic acid developed pruritis, thus the long term benefits and safety of this therapy need to be studied further.

The discovery of the role of a bile acid transporter (sodium taurocholate co-transporting polypeptide, NTCP) as a receptor for entry of hepatitis B and D is discussed under the section, ‘Clinical Relevance of Bile Acid Metabolism and Transport’. This update is

exciting and offers the potential for drugs to block viral entry into the hepatocyte. Furthermore, this discovery has resulted in a reliable cell culture system for these viruses.

Research into gut microbiome is being actively pursued now which has been discussed under the section, 'Interactions of Bile Acids and the Gut Microbiome'. Interactions of bile acid metabolism and gut microbiota in patients with cirrhosis are discussed in this section. Similar hypotheses are being looked at in the pathogenesis of inflammatory bowel diseases and hepatocellular carcinoma in these individuals.

Bile acid induced acute kidney injury in deeply jaundiced patients (cholemic nephropathy) is probably under-recognized clinically. Definition and methods to diagnose this condition are discussed in the section, 'Bile Acids are Metabolic Modulators'.

A variety of signals and receptor modulation in bile acid metabolism have been covered in the section, 'Therapeutic Potential of Bile Acids and Bile Acid Receptor Agonists'. Bile acid – farnesoid X receptor (FXR) – FGF 15/19 is an endocrine pathway, which opens up and targets to treat metabolic diseases and primary biliary cirrhosis. FXR agonists and FGF 19 analogues are in clinical trials now. In intrahepatic cholestasis of pregnancy, sulphated progesterone metabolites, by functioning as partial FXR agonists, may competitively inhibit bile acid homeostasis. Whether bile acid signal modulation can achieve benefits equivalent to bariatric surgery without the patient undergoing surgery is also discussed. However, it sounds a bit like science fiction at present!

Nor-ursodeoxycholic acid (nor-UDCA) is a derivative of UDCA with a methylene group deleted in its side chain. Nor-UDCA has physicochemical and therapeutic properties distinctly different from UDCA. It undergoes chole-hepatic shunting which enables targeting of biliary ductules. It also induces bicarbonate rich hypercholeresis which may be cholangioprotective. Direct anti-inflammatory, anti-lipotoxic, anti-fibrotic and anti-proliferative properties of nor-UDCA have been reported. The benefits of nor-UDCA in cholestatic and metabolic disorders are to be studied. Phase 2 trials of nor-UDCA in primary sclerosing cholangitis are awaited.

Overall, this book is a storehouse of knowledge on the new advances in bile acid signalling, its modulation and its clinical relevance. It is recommended for clinicians and researchers interested in the field of bile acids.

C. E. Eapen
Department of Hepatology
Christian Medical College
Vellore 632 004, Tamil Nadu, India
eapen@cmcvellore.ac.in