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Hepatic Encephalopathy: Analytical Methods of Interest in the Quantification of Therapeutic Agents Utilized in the Management of the Disease in Biological Fluids

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Editorial

Hepatic Encephalopathy (HE) is a neurological syndrome that is progressive but potentially reversible cause of cerebral dysfunction. The failure to detoxify ammonia and other nitrogen derived products predominantly found in the intestine is considered to be responsible for the pathogenesis of the disease [1]. The disease which can occur in patients with chronic liver disease and acute liver failure is associated with neuropsychiatric, cognitive and motor symptoms such as asterixis, ataxia, somnolence, bradykinesia, confusion, dysarthria, myelopathy, nystagmus, progressive alterations in muscular reflexes, seizures, transient focal deficits and coma [2,3]. The disorder has significantly contributed to increase in mortality of patients with cirrhosis [4]. Cirrhosis is a widespread disorganized nodules in the liver often combined with fibrosis. It can be compensated cirrhosis (liver continues to function) or decompensated cirrhosis (liver fails to function adequately). Hepatic encephalopathy is subdivided into type A (when associated with acute liver failure), type B (if connected to portosystemic bypass or shunting) and type C (when related to cirrhosis). Type C is classified into episodic (triggered by recognized risk factors), persistent (presence of chronic neuropsychiatric signs and symptoms) and minimal (diagnosed only with neuropsychological or neurophysiological tests) hepatic encephalopathy. Diagnosis can be accomplished by blood ammonia determination, computed tomography scans, magnetic resonance imaging of the brain and electroencephalogram triphasic waves [2].

The management of the hepatic encephalopathy in cirrhosis may include identification of triggering factors (constipation, gastrointestinal bleeding, hypokalemia, sepsis, uremia etc); eliminating probable causes of encephalopathy and treatment with therapeutic agents capable of lowering production and/or absorption of ammonia or enhancing its clearance. Some of the therapeutic agents that have been utilized for effective treatment of the disease include lactulose and lactitol (non-absorbable disaccharides), rifaximin (antibiotic), neomycin (rarely used currently due to nephrotoxicity and/or ototoxicity), metronidazole (antibacterial), flumazenil (benzodiazepine antagonist) and L-ornitine L-aspartate (LOLA, amino acids).

Effective treatment of disease can be assessed by measuring the drug concentration(s) in the biological fluids [5]. Measurement of drug concentration requires accurate, precise, sensitive, selective and specific analytical methods in order to accurately quantify the drug in biological fluids. Such analytical methods often used are spectroscopic and chromatographic methods. Among the chromatographic methods, high performance liquid chromatography or gas chromatography is mostly employed either as hyphenated or non-hyphenated system. Hyphenation is an on-line combination of a separation technique and one or more spectroscopic detection techniques. Biological fluids are very important to life and help maintain body homeostasis. Several biological fluids can be analyzed however, blood (whole blood, serum or plasma); urine; Cerebrospinal Fluid (CSF) are the ones very often analyzed for drugs content.

In the present article, it was considered an interest to examine analytical methods that determine these drugs used to treat hepatic encephalopathy in biological fluids. They include:

1. Rifaximin (an antibiotic) determined in (a) human plasma, Balasekhara et al. [6], Parka et al. [7], Blandizzi et al. [8] by hyphenated systems; Descombe et al. [9] by non-hyphenated system; (b) human urine, Blandizzi et al. [8] by hyphenated systems.

2. Metronidazole (antibacterial) determined in (a) human plasma, Ezzeldin et al. [10], Gulaid et al. [11], Emami et al. [12], Safdar et al. [13] by non-hyphenated system; Silva et al. [14] by

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hyphenated systems.

3. Flumazenil (benzodiazepine antagonist) determined in (a) human serum, Djordjević et al. [15] by hyphenated systems; (b) human plasma, Fisher et al. [16], Zedkova et al. [17], Chan and Jones [18] by non-hyphenated system Lavén et al. [19], Kratzsch et al. [20], Song et al. [21] by hyphenated systems.

4. L-ornitine L-aspartate (LOLA): determined in (a)Human plasma, Babu et al. [22], Schwarz et al. [23], Moller [24] by non-hyphenated system; (b) Human serum, Turnell and Cooper [25] by non-hyphenated system; (c) Human urine, Turnell and Cooper [25].

Conclusion

Drug metabolism depends on adequate hepatic function. Hepatic dysfunction, either acute (sudden onset) or chronic (extended duration) leads to diseases such as hepatitis (inflammation of the hepatocytes), fibrosis (increase in connective tissue in the liver), cholestatis (static bile flow), steatosis (fatty infiltration), necrosis (cell death) and cirrhosis (disorganized nodules in the liver combined with fibrosis) etc. Hepatic encephalopathy as one of the well-recognized complications of chronic liver diseases has been treated with the above-named therapeutic agents. Monitoring these therapeutic agents in biological fluids has been accomplished mostly by liquid or gas chromatography (HPLC OR GC). These chromatographic systems are often times combined with spectroscopic systems to enhance accuracy, precision sensitivity and selectivity. Finally, as these therapeutic agents are poorly absorbed into the systemic circulation, it will not be incorrect to suggest that hyphenated or non-hyphenated chromatographic analytical methods are the analytical methods of interest to be used in their quantification in biological fluids.

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