

PP16.1. HEPATOTOKSIČNOST U KLINIČKOJ PRAKSI: FARMACEUT KAO STUB BEZBEDNE TERAPIJE

M. Čulafić

Univerzitet u Beogradu – Farmaceutski fakultet, Beograd, Srbija

Hepatotoksičnost je najčešći razlog povlačenja lekova sa tržišta nakon registracije, a u kliničkoj praksi ostaje dijagnoza isključivanja, bez potvrdnog biomarkera. Podaci Prospektivnog evropskog registra oštećenja jetre izazvanog lekovima (engl. *drug-induced liver injury, DILI*) pokazuju da su najčešće implicirani antibakterijski lekovi (40%) i antineoplastici/imunomodulatori (27%), pre svega amoksicilin-klavulanat, flukloksacilin, atorvastatin, nitrofurantoin, infliksimab i inhibitori kontrolnih tačaka imunskog odgovora, dok je 7% slučajeva povezano sa biljnim preparatima i dijetetskim suplementima (uz podatke da taj udeo u drugim prospektivnim mrežama dostiže 20%). Predavanje ovom problemu pristupa iz perspektive kliničkog farmaceuta i povezuje realne prikaze pacijenata sa alatima primenljivim na primarnom i sekundarnom/tercijarnom nivou zdravstvene zaštite. Odabrani slučajevi ilustruju hepatocelularni, holestatski i mešoviti obrazac oštećenja klasifikovan pomoću *R* vrednosti, pri čemu svaki vodi kroz po jedan korak dijagnostičkog puta prema *EASL* smernicama: rekonstrukciju kompletne terapijske istorije uključujući *OTC* preparate i suplemente, procenu latencije i odgovora na obustavu leka, prepoznavanje *Hy*-jevog zakona i strukturiranu procenu uzročnosti primenom *RUCAM/RECAM* skale. Posebna pažnja posvećena je razlikovanju *DILI* od pogoršanja osnovne bolesti jetre i od prolaznog porasta transaminaza u okviru adaptacije, jer pogrešna atribucija jednako često vodi nepotrebnom ukidanju efikasne terapije koliko i propuštenom oštećenju. Biće predstavljeni dostupni resursi (*LiverTox, DILIRank*), kriterijumi za obustavu leka, intervali laboratorijskog praćenja i prilagođavanje doza prema sažetku karakteristika leka, uz osvrt na ograničenja *Child-Pugh* klasifikacije. Cilj je da farmaceut izađe sa primenljivim algoritmom za rano prepoznavanje i zbrinjavanje *DILI*.

PP16.1. DRUG-INDUCED LIVER INJURY IN CLINICAL PRACTICE: PHARMACIST AS A PILLAR OF MEDICATION SAFETY

M. Čulafić

University of Belgrade – Faculty of Pharmacy, Belgrade, Serbia

Hepatotoxicity is the most frequent reason for post-marketing withdrawal of medicines, yet in clinical practice drug-induced liver injury (DILI) remains a diagnosis of exclusion with no confirmatory biomarker. In the Prospective European DILI Registry, antibacterials (40%) and antineoplastic/immunomodulating agents (27%) were most often implicated, chiefly amoxicillin-clavulanate, flucloxacillin, atorvastatin, nitrofurantoin, infliximab and immune checkpoint inhibitors, while 7% of cases were attributable to herbal and dietary supplements (a share reaching 20% in other prospective networks). The lecture takes the perspective of a clinical pharmacist, linking real cases to tools applicable at primary and secondary/tertiary levels of care. Selected cases illustrate hepatocellular, cholestatic and mixed patterns of injury classified by the *R* value, each covering one step of the *EASL* diagnostic pathway: reconstruction of the complete medication history including over-the-counter products and supplements, assessment of latency and dechallenge, recognition of *Hy*'s law, and structured causality assessment using the *RUCAM/RECAM* scales. Particular attention is given to distinguishing DILI from decompensation of underlying liver disease and from transient transaminase elevation reflecting adaptation, since misattribution leads as often to unnecessary withdrawal of effective therapy as to missed injury. Available resources, drug-stopping criteria, laboratory monitoring intervals and dose adjustment based on the summary of product characteristics will be presented, together with the limitations of the *Child-Pugh* classification. The aim is that pharmacists leave with an applicable algorithm for early recognition and management of DILI.