

Is the indocyanine green clearance test useful in viral acute liver failure? Maybe!

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To the Editor,

the first cause of acute liver failure (ALF) in Western countries is acetaminophen intoxication, while viral hepatitis is responsible for the majority of ALFs in developing countries (1). HBV-related ALF can have two different etiologies: following an acute infection (A-ALF) or during a flare of chronic infection (C-ALF). C-ALF may occur spontaneously or as a result of the effect of chemotherapy or immunosuppressive agents (1,2). High titers of immunoglobulin M hepatitis B core antibody (anti-HBc IgM Ab) and lower viral loads are frequently found in A-ALF compared with C-ALF. Nucleoside analogues treatment need to be started as soon as possible regardless of the specific subgroup of HBV-related ALF (1-3). This therapeutic regimen is particularly relevant in patients considered for orthotopic liver transplantation (OLTx) to reduce the post-transplant HBV recurrence. OLTx is often the only available treatment to significantly improve the prognosis of HBV-related ALF.(1) However, the need for an emergency OLTx is challenging to decide. In numerous institutes, the indications of urgent liver transplantation for HBV-related ALF in non-cirrhotic patients are defined according to the King's College Criteria (KCC) (Table 1), which represent the current standard criteria, adjuvanted by the MELD scores (2,3).

However, if KCC specificity of 67–86% is acceptable, the 48–68% sensitivity makes, on the other hand, the effective decision making in urgent assessment for OLTx in HBV-related ALF patients difficult. (3)

We managed a case of HBV-related acute liver failure (ALF) in which the King's College Criteria were initially not completely met at the first patient evaluation. The MELD score and the other available biochemical parameters are summarized in table 2.

We performed on this patient the indocyanine green clearance test (ICG-PDR) that showed a very low PDR value of 1.7 %/min. Our multidisciplinary transplant team evaluated the clinical conditions and the results of laboratory tests, including the ICG-PDR value, led the decision to schedule an emergency liver transplantation. (4) Following subsequent clinical evaluation, the patient met also the KKC for transplantation. Two days later, the OLTx was performed with the complete recovery of the patient. Only few cases in the literature report the use of ICG-PDR in this setting. Recently, dynamic tests quantifying the liver functional status have been subject to increasing interest due to their prognostic potential in the early detection of liver failure in patients with native liver and recipients after OLTx (5). Indocyanine green (ICG) clearance assessment is a common and performant test to assess liver function (5,6). After intravenous injection, hepatocytes selectively uptake the ICG which is subsequently excreted into the bile in an ATP-independent process (5,6). The ICG does not enter the enterohepatic recirculation, so its elimination kinetics expressed as plasma disappearance rate (ICG-PDR) depends on liver blood flow, parenchymal cellular function, and biliary excretion (5,6). ICG-PDR is a complex measure of sinusoidal perfusion and

Table 1. Summarily King's College Criteria

Acetaminophene-associated ALF	All other causes of ALF
pH < 7.3	INR > 6.5
or	or
INR > 6.5, serum creatinine > 3.4 mg/dl, and grade III–IV encephalopathy	Three of the following variables:
	1. Age < 10 or > 40 years
	2. Cause is nonA, nonB hepatitis or idiosyncratic drug reaction
	3. Duration of jaundice before encephalopathy > 7 days
	4. INR > 3.5
	5. Serum bilirubin > 17.5 mg/dl

Table 2. Laboratory patients' results

Biochemical parameter	Italian ICU admission	PreOLTx
WBC, $\times 10^3$ /mCL	6.78	5.72
Hb, g/dL	10.2	10.8
Plts, $\times 10^3$ /mCL	172	177
PCR, mg/L	3.11	3.06
PCT, ng/mL	0.40	0.42
INR	2.65	4.53
Creatinine, mg/dL	0.88	0.91
AST/ALT, UI/L	115/528	87/459
Bilirubin tot./dir., mg/dL	19.12/9.01	18.779.95
Ammonium, mcMol/L	177	192
Na, mEq/L	149	149
K, mEq/L	4.83	3.53
pH	7.48	7.55
Lactates, mMol/L	3.5	2.5
HCO ₃ ⁻ , mEq/L	32.5	31.8

hepatocyte's membrane function, reflecting the functional reserve of undamaged hepatic-parenchyma. The test is performed bedside using transcutaneous pulse

densitometry, providing results within a few minutes (5,6). The literature reports as normal values major of 14-16% (5,7). One limitation to this procedure could be the spectrophotometric interference with high level of bilirubin, but using LiMON analyzer (Pulsion Medica System, Germany) this pitfall has been overcome due to its ability to measure ICG concentrations at two different wave lengths avoiding the interference coming from oxidized or reduced hemoglobin and from bilirubin due to the different peak of absorption (7). In our experience hemodynamic stability is imperative for reliable assessment of liver function.

This letter considers ICG-PDR value in difficult contexts such as HBV-related ALF to evaluate the residual liver function and guide the management of the patient.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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