EDITORIAL

Primary biliary cholangitis, let's try to keep the new nomenclature correct!

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It is only recently that the term primary biliary cirrhosis was changed into primary biliary cholangitis (PBC).[1] One of the main reasons to do so was because the former name did not reflect the natural history of the disease in the vast majority of today's patients.

When the disease entity of PBC was established, advanced liver disease showing histological and clinical findings of cirrhosis was found in most of the patients. Since the introduction of antimitochondrial antibodies for the diagnosis of PBC, the majority of patients are diagnosed in the early stages, well before the cirrhosis stage. As most of these patients with early stage PBC respond well to medical therapy, it is in just a minority of patients that the disease will eventually progress to cirrhosis.[1]

PBC is a chronic cholestatic disease of which the cause is still unknown. It is a slowly progressive autoimmune disease characterised by portal inflammation and necrosis of cholangiocytes in the small and medium-sized bile ducts. PBC has a strong female preference. The mean age at time of diagnosis is around 50 years.

Ursodeoxycholic acid (UDCA) is currently the only therapeutically effective agent for PBC. This drug does not cure but delays histological progression. After the introduction of UDCA in the 1990s the prognosis of PBC has dramatically improved. At present, two out of three patients diagnosed with PBC and treated with UDCA have an expected survival not different from the general population.[2] There is currently no consensus on how to treat patients with a suboptimal biochemical response to UDCA. Other drugs have been tested, but none have been found to be of benefit as single agent. The European guideline suggests a combination of UDCA and budesonide (6-9 mg/d) in non-cirrhotic patients (stages 1-3); however, the grade of evidence for this approach is low (grade III/C2).[3]

The biochemical response to UDCA after one year of treatment is an important indicator for the prognosis of PBC. Previous studies have shown that for patients fulfilling criteria for 'good biochemical response' the long-term outcome is significantly better than for non-responders. Non-responders remain at risk for requiring liver transplantation or premature death. Key papers with respect to the important prognostic information of biochemical response are those of Angulo et al.[4] and of Pares et al.[5]

This current issue contains a paper by Lammers et al. entitled 'How the concept of biochemical response influenced the management of primary biliary cholangitis over time'.[6] This is a retrospective study of a Dutch cohort of 851 PBC patients over a considerable period of time (1988-2011). The focus of this paper was to evaluate to what extent liver test results influenced patient management during a three-decade period, and whether this changed over time. In other words, if a patient was a non-responder on UDCA, was the therapeutic treatment modified in order to which this non-responder did respond effectively? For example, were other drugs added to UDCA? Unique to this cohort is that the study period includes both 1999 and 2006, the years in which the key papers with respect to the relevance of achieving good biochemical response were published. It could be expected that after these publications clinicians would be more aware of the importance of a good biochemical response and would adapt their clinical practice in the non-responders.

The authors found that management was modified in only a minority of the non-responders. They did not observe an increase of response-guided management over time. The most frequently seen modification was an increase in UDCA dose. Remarkably, budesonide was not added to UDCA in any of the non-responders.

I am not sure whether these somewhat 'disappointing' results are due to the lack of awareness among clinicians with respect to the concept of biochemical response. It seems logical to assume that this can mainly be explained due to the fact that we currently lack good second-line therapy. Fortunately, clinical trials are currently being

conducted and will hopefully result in effective alternative treatment within a short time. In the meantime, we cannot do better than to follow the guidelines in order to hopefully prevent cirrhosis from developing for both responders and non-responders. In order to try to keep the new nomenclature 'correct' for all patients with PBC.

REFERENCES

1. Beuers U, Gershwin ME, Gish RG, et al. Changing nomenclature for PBC: from 'cirrhosis' to 'cholangitis'. Gastroenterology. 2015;149:1627-9.
2. Kuiper EM, Hansen BE, de Vries RA, et al. Improved prognosis of patients with primary biliary cirrhosis that have a biochemical response to ursodeoxycholic acid. Gastroenterology. 2009;136:1281-7.
3. EASL Clinical Practice Guidelines: management of cholestatic liver diseases. J Hepatol. 2009;51:237-67.
4. Angulo P, Lindor KD, Therneau TM, et al. Utilization of the Mayo risk score in patients with primary biliary cirrhosis receiving ursodeoxycholic acid. Liver. 1999;19:115-21.
5. Pares A, Caballeria L, Rodes J. Excellent long-term survival in patients with primary biliary cirrhosis and biochemical response to ursodeoxycholic Acid. Gastroenterology. 2006;130:715-20.
6. Lammers WJ, Leeman M, Ponsioen CIJ, et al; on behalf of a Dutch Multicenter PBC Study Group. How the concept of biochemical response influenced the management of primary biliary cholangitis over time. Neth J Med. 2016;74:240-6.