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Hepatology Highlights

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Anti-parietal cell autoantibodies (PCA) in primary biliary cirrhosis: a putative marker for recurrence after orthotopic liver transplantation?

Ciesek S, et al. Efficacy of maintenance subcutaneous hepatitis B immune globulin (HBIG) post-transplant for prophylaxis against hepatitis B recurrence.

Singham, et al. Throughout most of its history, primary biliary cirrhosis (PBC) and chronic hepatitis B (HBV) , were considered the "yin and yang" of indications for liver transplantations.[1] Transplantation was considered virtually curative for the former disease and, until the mid-1990s, the latter was considered futile and an absolute contra-indication for transplantation due to a very high incidence of graft re-infection resulting in poor outcomes.[2] Needless to say, much has changed since the early days of transplantation. Graft recurrence of primary biliary cirrhosis is a well-recognized phenomenon[3-5] that usually occurs late post-transplant and is typically mild, although graft loss can rarely occur.[4] With the introduction of passive immunization with hepatitis B immune globulin (HBIG),[1] liver transplantation has become very feasible for those suffering from HBV. Initially most centers employed protocols requiring high dose intravenous HBIG,[6] however, the development of relatively effective antiviral agents has allowed for the use of combination prophylaxis protocols utilizing low dose intramuscular HBIG[7] in combination with oral antiviral agents. The low dose intramuscular HBIG protocols were an improvement in prophylaxis delivery that became more convenient, albeit sometimes painful, for patients and easier for the post-transplant clinic nursing staff. Today, liver transplant recipients undergoing transplantation for PBC and HBV enjoy excellent post-transplant outcomes.

In this current issue of the Annals, two liver transplant papers appear that explore post-transplant PBC recurrence and HBIG administration post-transplant even further. Dr. Ciesek and colleagues from Hannover Germany report an interesting paper studying the possible role of anti-parietal cell autoantibodies (PCA) as a marker for post-transplant PBC recurrence. PCA are well-known to be present in atrophic gastritis and can also be found in PBC. Ciesek et al reported that PCA were present in just under half of their PBC pre-transplant patients but appeared in 100% of liver transplant recipients with PBC recurrence. Although it remains to be explained why this has occurred, especially given the post-transplant immunosuppression that liver transplant recipients require (and Cisek et al did not find any significant differences in immunosuppressive regimins amongst their PBC recurrence patients), this finding has not been previously reported and is both hypothesis generating and worthy of future studies. With regards to post-transplant HBIG administration, Dr. Singham and colleagues from the University of British Columbia, report on a pilot study of a subcutaneous (SC) HBIG maintenance protocol. The SC protocol achieved the HBIG maintenance titres and was very well-tolerated. In fact, all of the patients enrolled in the SC protocol preferred the study protocol compared to their previous intramuscular protocol because of less pain at the injection site. Although a SC maintenance protocol will require further clinical studies before it can be considered standard of care, it may represent an improvement on existing HBIG protocols.

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Serum concentrations of substance P in cholestasis

Trivedi M, Bergasa NV. Both patients suffering from cholestatic liver disease (e.g. primary biliary cirrhosis) and their hepatologists/gastroenterologists are all too familiar with pruritis that ranges from mild to severe and debilitating. Relatively effective medications are often prescribed including rifampin[8] and, in rifampin-refractory cases, naltrexone.[9] Although these medications often work, sometimes surprisingly so, the truth is that they are prescribed empirically and clinicians do not know the precise cause/mediator of the pruritis of cholestasis. In this issue of the Annals, Drs. Trevedi and Bergasa, from the State University of New York and the New York Medical College respectively, report an interesting paper that studied the serum concentrations of substance P in pruritic patients with cholestatic liver disease, non-pruritic patients with cholestatic liver disease and a control group that did not have liver disease at all. Serum levels of substance P were markedly elevated in the cholestatic patients with pruritis but not in the two other comparator groups. Trevedi and Bergasa then followed this clinical study with an animal model utilizing rats that had undergone bile duct ligation. Again, they found that the rats that underwent bile duct ligation had elevated serum substance P compared to rats that did not undergo bile duct ligation. This interesting paper may shed some light on the mechanism of cholestatic associated pruritis. From a clinical perspective, it may also suggest a relatively simple laboratory test that can distinguish pruritis of cholestastic liver disease from the common non-liver disease causes of itching (ie. dry skin etc).

Pegylated interferon alfa 2b plus ribavirin for the treatment of chronic hepatitis C genotype 4 in adolescents

Al Ali J, et al. Hepatitis C (HCV) is a common infection throughout North America, Latin America and the rest of the world, a fact that is all too well known to the readers of the Annals. Many, many clinical trials of its treatment have been published as part of the drug registration process of interferon-based therapy in combination with ribavirin. HCV genotype 4, however, is relatively uncommon in North America and Latin America, but is a very common, as well as serious, clinical problem in the Middle East. Despite the fact that a few clinical studies of peginteferon and ribavirin in genotype 4 adult patients have been published from Egypt10 and Saudi Arabia,[11] the published outcomes of genotype 4 patients in the pediatric/adolescent population are distinctly rare. In this issue of the Annals, Dr. Al Ali and colleagues from the Kuwait University report on the outcomes of peginterferon and ribavirin combination therapy in a group of adolescents. Similar to the adult genotype 4 therapeutic experience,[10,11] the outcomes in the adolescent population are also excellent with a 75% sustained virologic response and excellent patient compliance. The publication of interesting paper, aside from its contribution to the pediatric hepatology literature, also signifies the truly international nature of the Annals and that the audience of the Annals is a world-wide one that goes well beyond North America and, Latin America.

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