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doi:10.1053/j.ajkd.2009.07.028

IN REPLY TO 'EVIDENCE OF OCCULT HEPATITIS C VIRUS INFECTION IN HEMODIALYSIS PATIENTS'

We read with interest the letter from Barril et al[1] commenting on our editorial,[2] in which we had suggested an absence of occult hepatitis C virus (HCV) infection in hemodialysis patients. Unfortunately, in their comments, the authors have not provided any additional convincing data, and many questions remain unanswered from their previous study, which reported that 45% of hemodialysis patients with elevated liver-enzyme levels of unknown cause had occult HCV infection, inducing an unusually high mortality rate.[3]

First, the authors have not provided the cause of death of these patients. Second, only 1 patient underwent a liver biopsy that showed isolated cholestasis, which is not specific for HCV infection. In another patient, liver cirrhosis was not biopsy proven. Third, they did not determine the cause of contamination; clinicians need to know how these patients were contaminated, and the hypothesis of nosocomial transmission has still not been demonstrated. HCV seroprevalence rates from the centers that participated in this study are also still missing. Finally, and surprisingly, the authors did not assess HCV RNA in patients with occult HCV infection who subsequently underwent a kidney transplant. In a previous study, we found no evidence of active HCV infection under immunosuppression in kidney transplant recipients who had been cleared of detectable serum HCV prior to transplant, a finding that argues against occult HCV infection in hemodialysis patients.[4]

Hence, in the absence of robust data, we still consider that there is no strong evidence to support the presence of occult HCV infection in hemodialysis patients.

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ACKNOWLEDGEMENTS

Financial Disclosure: None.

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doi:10.1053/j.ajkd.2009.09.002

INTRAMUSCULAR OR INTRADERMAL HEPATITIS B VACCINE ADMINISTRATION IN HEMODIALYSIS PATIENTS?

To the Editor:

In prevalent hemodialysis (HD) patients nonresponsive to a primary vaccination series, Barraclough et al[1] detected greater seroconversion rates with revaccination using intradermal (ID) administration of 5 μg of hepatitis B virus vaccine every week for 8 weeks (79%) in comparison to intramuscular (IM) administration of 40 μg of vaccine at weeks 1 and 8 (40%).

We have previously compared the response to IM versus ID vaccination in 31 incident HD patients. Engerix-B (GlaxoSmithKline Pharmaceuticals; www.gsk.com) was administered at 0, 1, and 2 months. Sixteen patients received 40 μg/dose of IM vaccination and 15 were assigned to receive 4 μg/dose of ID vaccination. Vaccination led to seroconversion of 62.5% of participants in the IM group and

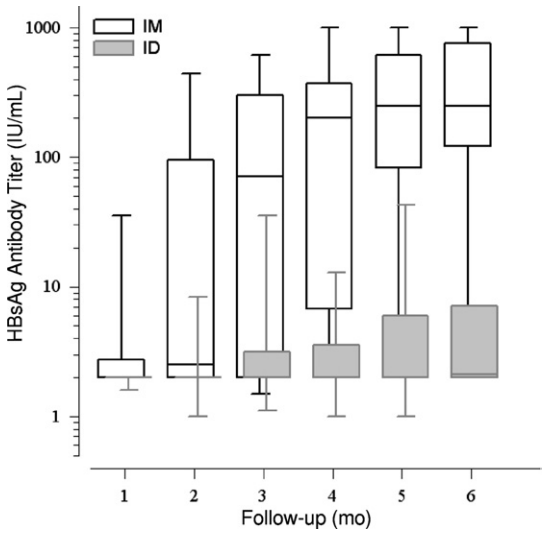

Figure 1. Comparison of seroresponse to intramuscular (IM) or intradermal (ID) administration of hepatitis B vaccine in incident hemodialysis patients. Abbreviation: HBsAg, hepatitis B surface antigen.

13.3% in the ID group. The study was interrupted by the Safety Monitoring Committee. Antibody titers to hepatitis B surface antigen during the observation period per group are shown in Fig 1.

Contrary to previous studies assessing stable patients for a longer treatment period, our cohort comprised patients who were starting on HD therapy. Moreover, it is possible that early interruption of the study prevented detection of significant differences that eventually may have arisen later. It also is possible that the lower response to ID inoculation occurred because of multiple factors; for example, there was some evidence of inflammation in this group, an observation with significance that cannot be discarded.

Thus, to explain the different responses obtained in our study versus that of Barraclough et al,[1] several possibilities might be considered: revaccination versus initial immunization, prevalent versus incident individuals, patient clinical conditions, characteristics of the populations at risk, or perhaps the different interval between vaccine and doses.

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ACKNOWLEDGEMENTS

The trial described in this letter is registered at www.ANZCTR.org.au as study ACTRN12609000616279.

Support: Dr Poli de Figueiredo is a researcher for Conselho Nacional de Desenvolvimento Científico e Tecnológico.

Financial Disclosure: None.

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doi:10.1053/j.ajkd.2009.07.024

IN REPLY TO 'INTRAMUSCULAR OR INTRADERMAL HEPATITIS B VACCINE ADMINISTRATION IN HEMODIALYSIS PATIENTS?'

Medeiros et al[1] contrast their data showing markedly lower seroconversion rates with intradermal (ID) compared with intramuscular (IM) hepatitis B virus vaccination with results from our trial[2] despite differences in study populations and trial methods.

First, in our trial, a major design feature was similar dose administration between groups. This excluded the potential confounding effect of total dose. In contrast, Medeiros et al[1] administered a markedly lower ID dose, raising the possibility that their low ID seroconversion rate may result from inadequate dose, rather than lower immunogenicity of the vaccination route.

Second, baseline comparison in our trial showed that the ID and IM groups were similar. Medeiros et al[1] comment on a higher inflammatory burden in the ID arm, ensuring an additional source of potential confounding.

Third, their study involved incident hemodialysis patients undergoing primary vaccination. We studied prevalent patients nonresponsive to a primary hepatitis B virus vaccination course. Given that their study participants were earlier in the course of renal disease and had not yet been declared as belonging to the more immunodeficient group of nonresponders, it would be expected that their cohort would be better able to mount a seroconversion response than ours. This does not account for the variable response in the ID versus IM arms, but makes direct comparison of overall seroconversion rates between the 2 study populations difficult and limits the applicability of our results to their cohort.

Because of the mentioned potential confounders, the relative merits of ID versus IM vaccination cannot be determined from the data of Medeiros et al.[1] In contrast, we believe that our study showed clear superiority of ID vaccination. Results should be generalizable to patients with clinical characteristics similar to those of our cohort.

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ACKNOWLEDGEMENTS

Financial Disclosure: None.

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doi:10.1053/j.ajkd.2009.08.009

ESTIMATED GFR FOR DRUG DOSING: A BEDSIDE FORMULA

To the Editor:

Stevens et al[1] showed that the Modification of Diet in Renal Diseases (MDRD) Study equation, after "uncorrec-