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Prospective study of hepatitis B vaccination in patients with chronic hepatitis C

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Chronic hepatitis C results in liver disease, cirrhosis, and hepatocellular carcinoma. Its prevalence is estimated to be 70-92% among intravenous drug misusers,¹ who are also at risk of parenterally or sexually transmitted hepatitis B. Coinfection with hepatitis B virus may accelerate underlying liver damage due to hepatitis C.²

Effective vaccines against hepatitis B have been available for a decade.³ Universal vaccination is being adopted in countries where hepatitis B is common. When vaccination has been targeted at promiscuous people and intravenous drug misusers uptake has been suboptimal and the incidence of hepatitis B has increased.⁴⁻⁵ We therefore investigated whether carriers of hepatitis C were being vaccinated against hepatitis B.

Patients, methods, and results

We prospectively studied 126 consecutive patients attending our hepatology clinic who had positive results for antibodies to hepatitis C virus in two second generation enzyme linked immunoassays (ELISAs; Murex Diagnostics, Dartford, and Sanofi Diagnostic Pasteur,

Guildford). Their median age was 38 years, and 86 were men. We documented demographic details including risk factors. Each patient was asked about the number of health service workers with whom they had had contact since they knew that they were positive for antibody to hepatitis C virus and whether they had been advised to be vaccinated against hepatitis B. Hepatitis B surface antigen, hepatitis B surface antibody, and hepatitis B core antibody were measured in Amerlite assays (Johnson and Johnson Diagnostics, Amersham).

Eighty eight patients were intravenous drug misusers, 22 had been exposed to blood or blood products, and 16 had no identifiable risk factor. Table 1 shows the results of serological tests for hepatitis B. Seventy five patients were negative for all serum markers of hepatitis B and were therefore still at risk; 52 of them had a history of drug misuse. None of the 75 patients had been offered vaccination, though they had seen an average of two doctors (range 1-4) and other healthcare professionals between being diagnosed as having hepatitis C and attending this clinic. Only nine of the 126 patients said that they had been advised to be vaccinated because of the risk of hepatitis B, and seven had followed this advice. Three further patients had been vaccinated because of travel or occupational risk.

Comment

In this series 41% of patients had been infected with hepatitis B (51/126), confirming the risk in carriers of hepatitis C. Only 7% (9/126) had been offered vaccination, although hepatitis B could have been prevented by

Table 1—Results of tests for hepatitis B markers in 126 patients with chronic hepatitis C

	No of patients	Comment
Hepatitis B surface antibody alone	3	All were vaccinated
Hepatitis B surface antibody and hepatitis B core antibody	12	7 were vaccinated
Hepatitis B core antibody alone	33	
Hepatitis B core antibody and hepatitis B surface antigen	2	
Hepatitis B surface antigen alone	1	
No marker	75	52 had history of intravenous drug misuse

this approach. Despite having contact with health workers, our patients said that they had not been advised about vaccination—though it may have been offered.

Little change has been observed in high risk behaviour among intravenous drug misusers, despite educational programmes. This population is difficult to identify in the community, and people who misuse intravenous drugs rarely approach healthcare professionals about vaccination. Sexual transmission of hepatitis B has increased in the United States, and the incidence of infection among misusers and their sexual contacts has probably increased.⁵

Our results suggest that opportunities for vaccination are being missed. The reasons that vaccination might

not have been offered include a failure to recognise that patients with hepatitis C are at risk of hepatitis B and a failure to appreciate that intravenous drug misusers have inconsistent contact with health care professionals. Some healthcare professionals may believe that vaccination is not their primary responsibility. Cost is unlikely to be an important issue as the vaccine is comparatively cheap and the current potential cost saving for the NHS in preventing acute or chronic hepatitis B undoubtedly offsets the costs of vaccination.

Patients with chronic hepatitis C who are at risk of hepatitis B should be offered vaccination at their first contact with health care professionals.

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Specificity of pH and osmolality of early morning urine sample in assessing distal renal tubular function in children: results in healthy children

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A simple method of evaluating distal tubular function in children would be useful because water deprivation tests are potentially dangerous and acid loading tests are unpleasant. Osmolality of an early morning urine sample is often taken as a measure of urinary concentration in children with a history of polydipsia and polyuria, and the pH of an early morning sample is used to evaluate urinary acidification in several renal and metabolic disorders. A pH of 5.4 or less is usually taken as adequate acidification¹ and an osmolality of 600 mmol/kg or more as excluding clinically significant impairment of urinary concentration.² We determined the likelihood of achieving these values in a single early morning urine sample from healthy children.

Subjects, methods, and results

We collected an early morning urine sample from 322 healthy children and adolescents (age range 3 years 11 months to 18 years 8 months, median 9.8 years; 170 males) from five local schools. The study was approved by the ethics and education management committees, and informed written consent was obtained from subjects or their parent or guardian. Subjects were asked to avoid drinking after going to bed, unless they found it uncomfortable to do so. No one had a personal or family history of renal or urinary tract disease or was receiving potentially nephrotoxic drugs. pH was measured with a digital pH meter and osmolality with a freezing point osmometer on the morning of collection. The cumulative distribution function was calculated for each value to determine the probability of observing a value above or below a specified point. Smoothing was performed by

means of Gaussian kernels.³ Reference ranges were determined from the resultant density estimates as the values between the 2.5th and the 97.5th centiles.

One child admitted to drinking after bedtime and eight to collecting the second urine sample of the day after breakfast; 313 (98%) subjects collected the first early morning sample. Osmolality was measured in all 322 samples and pH in 318. Median pH was 6.0 (range 4.8-7.7). The reference range was 5.16-7.07; only 12.8% of children had a value of 5.4 or less. Median osmolality was 845 mmol/kg (range 275-1344). Males had significantly higher osmolalities than females (median 896 v 781 mmol/kg; Mann-Whitney U test, $P < 0.005$); no sex difference was observed for pH. The reference range of urine osmolality was 417-1218 mmol/kg for the males and 329-1194 mmol/kg for the females; only 82.2% of males and 74.8% of females had an osmolality of 600 mmol/kg or more.

Comment

To our knowledge, this is the first study to establish reference ranges for osmolality and pH of an early morning urine sample in healthy children and adolescents after an overnight thirst, although these variables are widely measured by paediatricians and used in clinical assessment. The only other study of urinary concentration in normal children used a longer period of formal fluid deprivation.⁴ So far as we know, urinary acidification has never been studied in this way.

Our study clearly shows that not to have a urinary pH of 5.4 or less, or an osmolality of 600 mmol/kg or more, in a single early morning urine sample cannot be taken as evidence of impairment of urinary acidification or concentration because the specificity of these measures is low. Only about one child in eight will have a pH of 5.4 or less, making this an almost useless screening test. Although osmolality is more useful for evaluating urine concentration, only around four children out of five will have an osmolality of 600 mmol/kg or more. The use of early morning urine pH and osmolality is attractive in its simplicity, but failure to appreciate the limitations of these tests may lead to an incorrect diagnosis of distal tubular impairment.

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