Outbreak report

HEPATITIS B REACTIVATION IN AN IRISH DIALYSIS UNIT, 2005

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In April 2005, a case of reactivation of hepatitis B virus (HBV) infection occurred in a patient undergoing haemodialysis in an Irish hospital. This incident potentially affected patients attending hospitals throughout the country, so a national incident team was set up coordinate the response to the incident. A total of 306 dialysis patients, attending 17 different dialysis centres (14 in Ireland), were identified as having been potentially exposed to HBV as a result of this incident. A programme of HBV serological testing and HBV vaccination was instituted. There was no evidence that any patient acquired HBV infection as a result of cross-infection from the index patient, although 11 patients (3.6%) had evidence of past infection (anti-HBc positive, HBsAg negative). The majority of patients in this cohort were of unknown HBV vaccination status (62.7%), 13.4% were fully vaccinated, 4.6% partially vaccinated and 15.7% unvaccinated. Of 239 tested for anti-HBs, 183 (76.6%) had a titre <10 mIU/ml. Local incidents in dialysis units can have national implications due to the frequent patient transfer between units. This incident highlighted serious deficiencies in current structures and practices, and a lack of appropriate guidelines. However, there were positive outcomes from this incident. The majority of Irish dialysis patients have now been vaccinated against HBV, and lessons learned have been used to develop national guidelines on HBV vaccination and testing and on the management of incidents of blood-borne viral infections in dialysis units.

Introduction

Blood-borne viral hepatitis, in particular hepatitis B (HBV), has been recognised as a hazard for haemodialysis patients and staff since the 1960s [1]. The implementation of guidelines for the prevention and control of HBV infection since the 1970s, including HBV vaccination of patients and staff since the 1980s, has been associated with a reduction in incidence of HBV infection in dialysis settings [1-3]. Investigations of HBV outbreaks in dialysis units since the introduction of these guidelines have indicated that the major factors contributing to cross-infection include significant deficiencies in infection control practices and failure to vaccinate patients [4]. In Ireland, which is a low endemicity country for HBV, infections are notifiable diseases and national guidelines recommend HBV vaccination for patients with chronic renal failure [5,6].

In April 2005, a haemodialysis patient was identified as HBV surface antigen (HBsAg) positive, having tested HBsAg negative on commencing dialysis in November 2004. Laboratory investigation of an archived November 2004 sample, taken before the onset of the first dialysis, revealed that the patient was positive for HBV core

antibody (anti-HBc) and tested negative for hepatitis C antibody. Subsequent investigation also revealed that the patient had tested HBV positive in 1976. The April 2005 sample was negative for anti-HBc IgM and contained a viral load of 6.4×10^4 copies/ml. It was thought that these findings were caused by a reactivation of a previous HBV infection due to an immunosuppressive illness that developed subsequent to commencing dialysis. The patient was moved to an isolation facility and dialysed on a dedicated machine in April 2005. As the patient was potentially infectious from November 2004 to April 2005 and had been dialysed on several machines in the dialysis ward and was not isolated, there was concern that other dialysis patients may have been exposed to HBV.

A hospital incident team was set up and identified more than 300 adult patients as potentially exposed. A plan of communication, testing and vaccination was agreed on to investigate the incident. Although the majority of patients were still being dialysed in this hospital, some had returned to the care of other units in Ireland and abroad. Therefore, as the incident potentially affected patients in many regions and abroad, a national incident team, which included three members of the hospital team, was set up to co-ordinate the response.

Methods

Potentially exposed patients (primary cohort) were defined as patients haemodialysed in the index hospital, in the time period from the index patient's last negative HBsAg test to the date on which the index patient was isolated. One patient with pre-existing chronic HBV infection was excluded. As some inadequacies were identified in the index hospital's IT system, the national team verified the primary cohort by contacting all Irish adult dialysis units and relevant public health authorities abroad. As a complete list of dialysis units nationally was not readily available, the team compiled this using several sources. The lack of unique patient identifiers and robust IT systems in most units led to delays in identification of patients and necessitated the use of manual lists for organising testing schedules.

Parallel to compiling the list, the hospital incident team contacted each Irish adult dialysis unit to advise on their programme of HBV vaccination and testing. It recommended that all susceptible patients be offered an accelerated HBV vaccination schedule (40 mcg) and that HBV specific immunoglobulin (HBIG) be administered, as appropriate, to susceptible potentially recently exposed patients [1]. In addition, all primary cohort patients were to be tested for HBsAg weekly for 12 weeks from the date of last

dialysis within the exposure period in the index hospital [1]. This universal testing was necessary because information regarding HBV vaccination status and HBV surface antibody (anti-HBs) titre was not readily available for the majority of patients. For primary cohort patients not currently on haemodialysis, monthly rather than weekly HBsAg testing was recommended for patient convenience. In addition, as patients could have acquired HBV and subsequently lost HBsAg, it was recommended that they be tested for anti-HBc to ensure that recent HBV infection had not occurred. Hereafter, the national team contacted each Irish dialysis unit to clarify the recommended testing and vaccination schedules, and to enquire about past protocols and practices for testing and vaccination. In addition, a written protocol for the management of any new cases of HBV infection related to this incident was developed. In June 2005, it became apparent that the full range of recommended tests had not been carried out on all primary cohort patients for a variety of reasons, so the national team recommended that in these cases the last specimen of the testing programme be tested for both HBsAg and anti-HBc.

Data on the primary cohort were collected at intervals during the testing period from dialysis units and laboratories using a unique identifier. Demographics and details regarding dialysis, past HBV infection and vaccination, post-incident vaccination and laboratory investigations were recorded on a Microsoft Access database. Where a full range of testing had not been carried out, an attempt was made to establish the reason for this.

A final status was assigned to each patient as follows:

- ▶ HBV-infected (either new positive HBsAg result, new positive anti-HBc result when archived samples were anti-HBc negative or a positive anti-HBc IgM during or after the potential exposure period);
- ▶ past HBV infection (negative HBsAg, positive anti-HBc on an archived sample pre-dating November 2004);
- ▶ not infected (full range of recommended tests negative);
- ▶ other (full range of recommended tests not done).

Results

Some 306 primary cohort patients, in 17 dialysis centres (14 in Ireland and three elsewhere in Europe) were identified. Nearly half were 65 years or older; 190 were male. Two hundred and sixty (85%), were currently on haemodialysis; 18 had resolved acute renal failure, 16 had received a renal transplant, and six were on continuous ambulatory peritoneal dialysis (CAPD). Six were of unknown treatment status.

Previous protocols

A variety of strategies for HBV vaccination and testing were in place in the Irish units prior to this incident. Five units had a routine vaccination programme, seven had none, one had a programme that was not yet activated and one unit routinely asked GPs to vaccinate but few patients had been vaccinated. Regarding pre-dialysis laboratory screening, 13 units tested HBsAg and one tested both HBsAg and anti-HBc. All tested HBsAg every two to three months thereafter. Ten units reported that they had a tracking system whereby patients' dialysis sessions could be tracked to particular machines and staff members. The detail of these systems was not investigated.

Results of laboratory testing

A final HBV serological status was assigned to all patients (Table 1). A total of 2,938 HBsAg tests were performed. Seven patients had vaccine-related weak positive HBsAg test results that occurred within 13 days of vaccination and all were negative for both HBsAg and anti-HBc on follow-up investigation. Apart from the weak positive HBsAg results described above, no patient tested positive for HBsAg over the testing period.

TABLE 1

Final HBV status of primary cohort patients

Final Status	Patients	%
Not infected	278	90.8
Past infection	11	3.6
Other	17	5.6
HBV infection as a result of the incident	0	0
Total	306	100

Eleven patients were found to have past HBV infection (anti-HBc positive, HBsAg negative) based upon serological results on archived and recent samples. There was no serological evidence that any patient acquired HBV infection as a result of cross-infection from the index patient

Seventeen patients did not complete the full range of recommended tests. Eleven had no HBsAg tests after the incident (seven had died, three were uncontactable and one refused testing). Two patients who subsequently died each had one HBsAg test after the incident. Two patients had nine and seven HBsAg tests respectively, with the last one more than 10 weeks from the date of last dialysis in the index hospital and it was therefore considered unlikely that they could have acquired an infection. One patient had six and one had two HBsAg tests (the last test six and eight weeks respectively after last dialysis in the index hospital).

HBV vaccination status and anti-HBs titres prior to the incident

Anti-HBs titres at the start of this investigation, or in the three months prior to it, were available for 239/295 (81%) patients (having excluded those who were subsequently shown to have past infection). The majority, 183/239 (76.6%), had an anti-HBs titre <10 mIU/ml; 30 (12.6%) had a titre of 10-99 mIU/ml and 26 (10.9%) ≥100 mIU/ml. Only 41 patients were reported to have completed a HBV vaccination schedule prior to the incident and fourteen had a history of partial HBV vaccination (Table 2).

TABLE 2

HBV Vaccination status of primary cohort patients prior to the incident

Prior HBV Vaccination Status	Patients	%
Full	41	13.4
Partial	14	4.6
None	48	15.7
Unknown	192	62.7
Prior HBV infection	11	62.7
Total	306	100

TABLE 3

Anti-HBs results (February–April 2005) of patients with full HBV vaccination prior to the incident

Anti-HBs results (mIU/mL)*	Patients	%
<10	3	7.3
10–99	18	43.9
≥100	18	43.9
Unknown	2	4.9
Total	41	100

*Anti-HBs levels tested between February and April 2005

Thirteen anti-HBc negative patients, 10 of whom were reported as of unknown vaccination status and three as not having been vaccinated, had anti-HBs levels ≥10 mIU/ml and therefore were likely to have been vaccinated previously.

Anti-HBs levels in February–April 2005 were available for 39/41 patients with completed HBV vaccination, with the majority (36 patients) having anti-HBs ≥10 mIU/ml (Table 3). Documented post-vaccination anti-HBs levels (within two–four months of the final HBV dose) were available in 16/41 patients. This was ≥100 mIU/ml in 10 patients, 10–99 mIU/ml in three, and three did not respond to HBV vaccination. Of the 17 patients with information indicating partial vaccination prior to the incident, seven had anti-HBs levels ≥10 mIU/ml.

HBV vaccination following the incident

Thirty-six patients were identified as requiring HBIG: of those, 30 received it, three were offered it but refused, and a further three were not offered it. Regarding the Hepatitis B vaccination, most patients received the higher vaccine dose (40 mcg), and an accelerated preliminary schedule, either 0, 7, and 21 days, or 0, 1, and 2 months. Excluding the 11 patients with past HBV infection, and the 41 who were fully vaccinated before the incident, the vaccination status of the remaining 254 at five months was: 186 (73.2%) fully vaccinated, 10 (3.9%) currently being vaccinated, 14 (5.5%) deceased, 4 (1.6%) not vaccinated as they had protective anti-HBs levels, and 40 (15.7%) unvaccinated patients. Of the 40 unvaccinated patients, 32 were no longer on dialysis, six refused vaccination, one had a reported contra-indication to vaccine and one was not on dialysis anymore and could not be contacted. In addition to the primary cohort, most units had also used this opportunity to vaccinate their other dialysis patients.

Discussion

This incident highlights the fact that a case of HBV infection in one haemodialysis unit may impact on patients in dialysis units throughout Ireland and also abroad. Fourteen of 16 adult dialysis centres in Ireland (87%), and three centres outside the country, were affected.

During the investigation, it became clear that there were difficulties in the identification and follow up of the cohort, due to the lack of unique patient identifiers and suitable national IT systems. As a result, some patients were not tested according to the recommended schedule and some patients who were immune to HBV were tested unnecessarily. We recommend that a standardised national information system be implemented to address the complex needs of haemodialysis patients, including a “Smart card” containing basic demographic data, results of laboratory tests and

HBV vaccination status. This will facilitate information transfer during movement of patients between dialysis centres nationally and internationally.

Although guidelines for the prevention and control of blood-borne viruses (BBV) in haemodialysis units published in other countries have served as a resource for Irish practitioners [1,3], the lack of such national guidelines has led to variation in HBV testing and vaccination protocols throughout the country. Most units followed UK guidelines which advise HBsAg, but not anti-HBc, testing before the onset of the first haemodialysis and three-monthly thereafter [1]. In the US, HBsAg and anti-HBc are tested pre-dialysis, with monthly HBsAg for susceptible patients and annual anti-HBs for vaccinated immune patients [3]. Only a third of the Irish units had a programme of routine HBV vaccination in place, despite the recommendation of the national immunisation guidelines that patients with chronic renal failure should receive HBV vaccination [5]. The national team used experiences gained during management of this incident to contribute to detailed guidance on HBV vaccination and testing which was incorporated into a chapter on blood-borne viruses in the haemodialysis, CAPD and renal transplant setting in the national guidelines on the prevention of transmission of BBVs in healthcare settings [4].

Due to the successful implementation of the testing programme following the incident, it was possible to assign a final status for most (94%) patients. There was no evidence that any patient became infected with HBV. This probably reflects the good standards of infection control practices within the Irish dialysis units. Transient weak positive HBsAg results occurred in seven patients post-vaccination. While this occurrence has been previously reported [7–12], it presented specific challenges during this incident, in terms of interpretation of results, patient concern and infection control. Although this problem would have been avoided by testing for HBV DNA, rather than HBsAg, DNA testing was not feasible in this incident due to cost, the need to obtain timely results, and the logistics of collecting suitable samples. Eleven (3.6%) patients were found to have evidence of past HBV infection. This is the first time information has been available on HBV infection in Irish dialysis patients. The identification of previously unidentified patients with past HBV infection raised issues of patient counselling and of the appropriate management of HBsAg negative, anti-HBc positive dialysis patients. This is not addressed in the current UK guidelines [1]. While US guidelines recommend HBV DNA testing, they do not propose any viral load cut-off point above which patients require segregation, but rather recommend that isolation is not necessary once HBsAg remains negative [3]. Neither guidelines proved useful regarding advice on follow-up HBsAg testing. As with the index patient, such patients could potentially reactivate HBV infection due to immunosuppression, have detectable HBsAg and be potentially infectious. We recommended that these patients should be tested monthly for HBsAg but did not need to be isolated once HBsAg remained negative. However, this issue should be addressed in future haemodialysis guidelines; in particular, consideration should be given to the need to dialyse these patients in isolation. We recommend that all patients are tested for anti-HBc pre-dialysis.

The proportion of haemodialysis patients who develop a protective antibody response (≥10 mIU/ml) after HBV vaccination has been reported to be lower than in adults with normal immune status: median 64% (range: 34–88%) after a three-dose schedule and 86% (range: 40–98%) after a four-dose schedule; this compares with a protective anti-HBs response in 90–95% of those with normal

immune status after a three-dose schedule [3]. Our finding that 36/41 (88%) patients vaccinated prior to the incident still had protective anti-HBs, with an anti-HBs level ≥ 100 mIU/ml in half of these, clearly indicates that vaccination of these patients is a worthwhile exercise. Some studies have demonstrated that higher antibody response rates could be achieved by vaccinating patients with chronic renal failure before they become dialysis-dependent [3].

No cases of HBV cross-infection were identified. However, given the susceptibility of the cohort there was the potential for a more serious outcome. The investigation and management of this incident was time-consuming and costly and represented a significant additional workload for hospital, laboratory and public health professionals, much of which might have been avoided by prior vaccination and a national haemodialysis services IT system. The incident highlighted several serious deficiencies in current structures and practices that should now be addressed in order to avoid or minimise the potential for serious BBV transmission in the future. Positive outcomes are that the majority of dialysis patients are now vaccinated, and lessons learned from this incident have informed the updating of national guidelines on HBV testing and vaccination in the haemodialysis setting.

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