AIDS virus antibody in polytransfused dialysis patients vaccinated against hepatitis B

Patients receiving long term haemodialysis are at increased risk of hepatitis B infection. Given the similar transmission routes of hepatitis B virus and the virus of the acquired immune deficiency syndrome (AIDS) it is surprising that no seroprevalence data on infection with lymphadenopathy associated virus/human T cell lymphotropic virus type III (LAV/HTLV-III) in dialysis centres have been published. We present data from 18 haemodialysis centres in Belgium, where we surveyed all patients who had received at least three doses of hepatitis B vaccine. These centres had had a high incidence of hepatitis B infection before vaccination.[1]

Patients, methods, and results

At the end of 1985 serum samples were obtained from 729 patients receiving haemodialysis (335 (46%) men, 394 (54%) women). These patients received three to nine (mean 4·2) doses of plasma derived hepatitis B vaccine, some beginning in 1981.[1] They had been dialysed in 18 centres in Belgium for an average of 37 months. Pasteur vaccine (six lots) had been given to 488 patients (67%); CLB (Centraal Laboratorium voor de Bloedtransfusie, Dutch Red Cross) vaccine (two lots) to 146 (20%); MSD (Merck Sharp and Dohme) vaccine (one lot) to 29 (4%); and an assortment of the above vaccines to the others. About 90% of patients had received blood transfusions. In 1981, 46% of patients were transfused over six months,[1] and this practice had essentially been maintained.

Screening for anti-LAV/HTLV-III by the Abbott enzyme linked immunosorbent assay gave a positive finding in 33 patients (4·5%) and the result remained positive on repeat testing in 17 (2·3%). In no case detected by screening could the result be confirmed by immunofluorescence, Western blot, or the Wellcome competitive enzyme linked immunosorbent assay, and results were also negative with the new Abbott recombinant envelope/core competitive confirmatory enzyme linked immunosorbent assay. Most false positive results could be explained by cross reactivity in the Abbott screening assay of antibody against lymphocyte (HLA) components elicited by transfusion.[2]

Comment

Our findings in polyvaccinated, polytransfused patients show the complete safety from AIDS of all hepatitis B vaccines sold in Europe, regardless of methods of manufacture. They also show that blood transfusion in Belgium has remained very safe. The spread of the AIDS virus in Belgium has been late and slow, despite the many diagnoses of AIDS in visitors to Belgium. Since 1982-3 risk groups have been barred from donating blood, and since August 1985 all donations have been screened for antibody. According to a provisional estimate of the Belgian AIDS Commission, about five in 100 000 donors in 1985 were true positives for the antibody.

The evidence that patients with renal insufficiency seroconvert and may develop symptoms of AIDS virus infection comes from patients grafted with infected kidneys[3-5] and not from those exposed either to occasional true seropositive subjects who enter dialysis programmes or to blood transfusions. No proof of transmission of the AIDS virus during haemodialysis has been published, which is in sharp contrast with the easy spread of hepatitis B virus in this setting.

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Renal cell carcinoma: blood transfusion and survival

Data indicating that blood transfusion may be a significant risk factor in the prognosis of colonic cancer were reported in 1982 and 1985.[1,2] No causal association was claimed for this observation, but it is thought that homologous blood transfusion may cause immunosuppression, which might explain the improved survival of kidney grafts after transfusion.[3] We performed a retrospective analysis of transfusions and death due to recurrence in patients with surgically curable renal cell carcinoma.

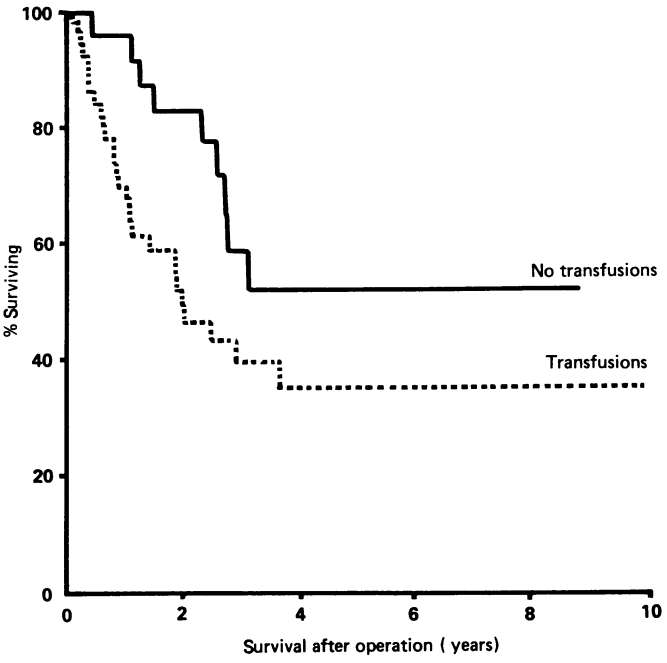
Patients, methods, and results

We examined the records of patients who had undergone nephrectomy for renal cell carcinoma during 1975-85. Age, sex, presenting symptoms, date of operation, site of tumour, tumour stage, haemoglobin concentration and packed cell volume on admission, details of blood transfusions, duration of follow up, use of chemotherapy or irradiation, and recurrence of tumour or death were recorded. We selected all patients considered to be potentially curable by surgery and therefore excluded (i) those who presented with metastases; (ii) those found at operation to have nodal disease; and (iii) those whose carcinoma was beyond stage pT3 or V1. A total of 80 patients met these criteria.

A binary variable was used to indicate whether each patient had or had not been given a blood transfusion, as the death rate among patients who had received transfusions seemed to be constant regardless of the timing of the transfusion, the number of transfusions given, and the total number of units transfused. Altogether 55 patients had received perioperative blood transfusion.

We used the tumour classification of the International Union Against Cancer (1978). Fourteen patients had stage pT1 disease, 41 stage pT2, and 25 stage pT3. The incidence of transfusion in these three staging groups was 21% (3/14), 76% (31/41), and 84% (21/25) respectively.

Owing to the inexact nature, timing, and measurement of recurrence and the fact that recurrence inevitably led to death in these patients we used survival time rather than the time to recurrence in the analysis. Distributions of the survival times were estimated for patients who had received transfusions and those who had not using the Kaplan-Meier product limit method.[4] Those who died from other causes and those who survived until the end of the study were treated as censored data (figure). The difference in the survivor functions was significant using the Mantel-Cox statistic (p=0·04).



Survival of patients who had and had not received transfusions.

A series of Cox proportional hazards models were fitted using all baseline factors except transfusion state as covariates.[5] Only the stage (pT) of tumour was a significant factor ($p<0·05$). When transfusion state was added to the proportional hazards model as an additional covariate the log likelihood was increased by 0·30. The test statistic, derived as $2\times0·30$ and compared with a χ^2 distribution with one degree of freedom, was not significant. We therefore concluded that blood transfusion has no significant effect on survival time once the stage (pT) of tumour has been accounted for.

Comment

In this study a simple comparison between patients who had and had not received transfusions suggested that transfusion has a significant ($p=0{\cdot}04$) adverse effect on survival time. When adjustments were made for other prognostic factors, notably the tumour pT stage, however, it became obvious that transfusion was not a significant predictor of survival in patients with renal cell carcinoma.

These results do not confirm the results found in patients with colorectal cancer. We suggest that other cancers should be assessed along similar lines.

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Industrial exposure to hydrogen cyanide: implications for treatment

We had the opportunity of studying nine patients exposed to hydrogen cyanide in a single incident at an industrial plant and three other patients exposed in separate incidents. We believe that our observations have important implications for treatment of such patients.

Patients and outcome

A suspected leak from a valve allowed hydrogen cyanide to escape. Nine men developed symptoms compatible with cyanide toxicity, of whom three lost consciousness. None of the men had definitely identified the "bitter almonds" smell said to be characteristic of hydrogen cyanide. The symptoms experienced included lightheadedness (eight men), breathlessness (eight), feeling shaky (six), headache (four), and nausea (four). The three unconscious men rapidly recovered consciousness after being moved from the area where they had been working. All nine men were attended by the works medical officer on site and then taken to hospital. All patients either showered or bathed, and oxygen was administered. Arterial blood was sampled and whole blood samples analysed for cyanide[1] (table).

Mean pulse on admission was 104 (SEM 4) beats/min, mean systolic blood pressure 140 (8) mm Hg, and mean diastolic blood pressure 84 (5) mm Hg. These figures, however, include the values found in three patients who showed relative hypotension—that is, systolic blood pressure 20-30 mm Hg below its normal value (nadir values 90, 100, and 110 mm Hg)—for up to three hours after admission. These three men included two of those who had been unconscious. Four patients had headache that persisted for up to eight hours after admission. There was no clearcut relation between blood cyanide concentrations on admission and symptoms, although the three patients who had lost consciousness had the highest concentrations (table).

Biochemical findings in patients exposed to hydrogen cyanide

Case No	pH	Carbon dioxide tension (kPa)	Bicarbonate (mmol/l)	Oxygen tension (kPa)	Cyanide (μmol/l)	
					On admission to hospital	One month after incident
1*†‡	7·40	3·2	19	34·3	115	11
2*	7·44	3·7	23	16·3	130	6
3*†‡	7·34	3·2	24	49·1	104	5
4	7·35	5·1	22	12·3	35	5
5	7·41	4·0	22	11·1	57	5
6	7·42	4·7	24	11·2	96	7
7†	7·40	4·1	22	11·2	50	9
8	7·37	5·1	23	10·4	67	3
9	7·38	4·7	23	9·3	41	3

*Patients initially unconscious.
†Patients with relative hypotension.
‡Patients receiving high flow oxygen when blood was drawn.
Conversion: SI to traditional units—Oxygen and carbon dioxide tensions: 1 kPa≈7·5 mm Hg. Bicarbonate: 1 mmol/l=1 mEq/l. Cyanide: 1 μmol/l≈2·7 μg/100 ml.

Three other men were also treated in separate incidents between 1970 and 1984 after exposure to hydrogen cyanide. Two were unconscious, although both regained consciousness rapidly. Cyanide concentrations in blood taken about 30 minutes after exposure were 284 and 173 μmol/l (768 and 467 μg/100 ml) in the patients who lost consciousness and 59 μmol/l (160 μg/100 ml) in the other patient.

Comment

All of our patients had absorbed appreciable amounts of cyanide, as shown by their blood cyanide concentrations. One of the problems in interpreting previous reports is that blood concentrations were measured in only a few patients after short term exposure to hydrogen cyanide, experience at Billingham being the exception (D D Bryson, personal communication). It has been suggested that cyanide concentrations above 111 μmol/l (300 μg/100 ml) are potentially lethal,[2] yet four of our patients had values above this. Thus blood cyanide concentrations are not accurate in predicting severity of toxicity and should be used only to confirm that appreciable cyanide absorption has occurred, not to determine treatment.

The most important lesson to be learnt is that patients can recover spontaneously and quickly from apparently severe poisoning with hydrogen cyanide, as shown by the five patients who lost consciousness: their conscious level had largely returned even in the short time before the arrival of the works medical officer (probably less than 10 minutes). This emphasises the importance of making the decision to give antidotes to cyanide on clinical grounds and on the basis of the patient's changing condition, particularly his conscious level.[3] Our experience suggests that if the patient has been removed from the area of exposure and further absorption of hydrogen cyanide prevented then even if he is unconscious an antidote does not have to be administered immediately unless the vital signs are deteriorating. Caution in giving antidotes to cyanide, particularly dicobalt edetate, the most popular antidote in the United Kingdom, is advisable because of their potential toxicity.[3,4] Clearly, appropriate supportive care must be begun immediately: several severely poisoned patients who have ingested potassium cyanide have recovered after being given full supportive measures but no antidote.[2,5] Most probably any patient exposed to hydrogen cyanide who reaches hospital fully conscious will require merely observation and reassurance.

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Haem arginate in the treatment of acute hepatic porphyrias

Haematin has been used for 15 years to treat acute porphyric attacks. Its disadvantages are instability in solution, harmful effects on coagulation, and thrombophlebitis.[1-3] For these reasons safer, more stable preparations have been developed. We report the effects of haem arginate, a new haem preparation, in patients with acute intermittent porphyria and variegate porphyria.