

Prevention of Transfusion Hepatitis

By

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(Received April 3, 1963)

It is generally recognized that hepatitis is a serious late complication of transfusions of blood or plasma, which have found widespread and effective application in modern therapy. The incidence of hepatitis following such transfusions suggests that some 2 to 3 per cent of the blood donors are harbouring the virus [1]. While gamma globulin is widely employed in the prevention of oral infection by virus A and is effective even in small doses, it is not in general use in the prophylaxis of transfusion hepatitis, since it is thought that hepatitis caused by the B virus cannot be prevented by gamma globulin.

Previous work on this problem was reported by NEEFE et al. [2]. These authors showed that the administration of two 10 ml doses of gamma globulin within one month to wounded soldiers treated with blood transfusions reduced the incidence of hepatitis to one third of that in the control group. A single injection of gamma globulin prolonged the incubation period.

Our own previous work [3, 4] demonstrated that a prolongation of the incubation period could be

achieved by subjecting the A virus to preliminary mild alcohol treatment and injected into children with a corresponding quantity of gamma globulin. The results of these experiments were explained at the time as being due to the gamma globulin administered with the virus, a view also held by NEEFE et al. [2]. It is thus possible that some cases of transfusion hepatitis are caused by the A virus; the prolonged action of the incubation period in this instance would be due to the effect of the A antibody present in the blood or plasma. The idea arose that transfusion hepatitis caused by A virus might be prevented by administering large quantities of gamma globulin.

MATERIAL and METHODS

Premature infants were chosen for the experiments. They receive many blood and plasma transfusions, with a high incidence of subsequent hepatitis, and, furthermore, small quantities of gamma globulin are sufficient to provide the required antibody level. The mechanism of prevention is also easily understood in premature infants, since they do not produce antibodies and thus only passive immunity is involved in their protection.

For the study such infants were selected who had received transfusions of blood after the tenth day of life. Their birth weight ranged from 1100 g to 2000 g. The gamma globulin used (Production and Research Institute for Serobacteriology "Human", Budapest) contained 10 per cent protein. The usual dose of it was 8 ml/kg body weight, injected into the thigh muscles in 2 to 3 divided doses either the day before or the day after the first transfusion of blood.

A control group (Control I) received blood transfusions but no gamma globulin. A second group (Control II) had regular premature infant care with vitamins, etc., but did not receive either blood transfusions or gamma globulin. General care was identical in all the three groups. The infants were treated at the hospital, at the same time.

RESULTS

Our study extended over a period of two years and included 182 premature infants to whom gamma globulin was administered and who survived for at least one year. Each infant received an average of 82 ml of blood or plasma, the number of transfusions varied between 3 and 13 with a mean of 5.3. The plasma for the transfusion was always prepared from the blood of one single donor and not from pooled blood. The series of transfusions was completed within 40 days after the administration of gamma globulin in 61 per cent, and within 70 days in 80 per cent, of the cases. The remaining 20 per cent of the infants continued to receive transfusions after 70 days.

Of the patients who had received gamma globulin with the first transfusion, only one contracted hepatitis.

TABLE I
Summary of experimental results

	Gamma globulin 8 ml/kg	Control I	Control II
Number of cases studied	182	205	204
Number of transfusions (mean)	5.3	5.7	0
Volume of transfusions (ml)	82	102	0
Per cent of cases receiving last transfusion 40 days after gamma globulin	61	—	—
Per cent of cases receiving last transfusion 70 days after gamma globulin	80	—	—
Days in hospital (mean)	71	69	70
Number of cases of hepatitis	1	15	0

The intervals between the first and last transfusions and the onset of hepatitis were 72 days and 39 days, respectively. Which of the four transfusions given had been responsible for the infection, could not be determined with certainty.

Control group I consisted of 205 premature infants. Although the average volume of blood transfused somewhat exceeded that given to the experimental group, the number of transfusions, a fact of more importance in the transfer of infection, was almost identical. The periods spent under hospital care were also similar in these two groups. The two groups were thus comparable in general condition, degree of prematurity and viability. In control group I, 15 cases of hepatitis were detected, an incidence of hepatitis of 1 for every 80 transfusions (1.2 per cent). This figure

is comparable with those reported in the literature.

With the exception of 3 cases [1, 7, 15], the patients received a number of transfusions close to the average. Which of the transfusions had been the source of infection could not be determined because of the length of the period over which transfusions had been administered. It was most likely, however, that Cases 9 to 15 shown in Table II had hepatitis of virus B origin, while in the patients 1 to 8 A or B virus could be considered the cause of hepatitis. However, since in case 2 the maximum incubation period was 56 days, the case can be considered as an infection by virus A.

The only case of hepatitis to occur after the administration of gamma globulin is recorded at the bottom of Table II. The possible incubation period in this case was between 39 and 72 days. The last transfusion was given 32 days after the injection of gamma globulin.

In control group II none of the 204 premature infants developed hepatitis.

DISCUSSION

The results of our experiments show that the occurrence of transfusion hepatitis can considerably be reduced by the administration of large quantities of gamma globulin. The explanation of this effect is not clearly understood, the view commonly presented in the literature being that the majority of cases of hepatitis following transfusions are due to virus B and that gamma globulin is ineffective against virus B.

If we accept that virus B has a dominant role in transfusion hepatitis, then, according to our results, protection can be achieved with large doses of gamma globulin even in virus B infections. This is only possible if the blood used for the preparation of the gamma globulin contained specific antibody against virus B. This specific antibody could be present in the gamma globulin if some of the donors had experienced a virus B infection and their sera consequently contained the antibody. Another possible explanation is that virus A shares a common antigenic factor with virus B, so that the blood of persons who

TABLE II
Hepatitis following transfusions

No.	Initials	Volume (ml.)	Number	Possible incubation period, days
		of transfusions		
1	V. G.	545	34	3—163
2	K. Zs.	145	6	17— 56
3	Cs. A.	208	8	24—116
4	S. J.	145	5	37— 76
5	B. M.	162	8	46— 95
6	F. Z.	280	4	59—118
7	B. E.	216	11	60—139
8	B. K.	115	7	60—139
9	K. M.	90	4	68— 78
10	K. L.	95	4	72—128
11	L. Cs.	305	4	80—111
12	K. J.	50	3	90— 92
13	V. E.	120	6	90—130
14	M. D.	46	3	95—101
15	T. E.	300	13	105—245
16	M. M. received g. gl.)	55	4	39— 72

have had virus A infection contains antibodies effective against virus B, too, even if in lesser amounts. In this case sufficiently large doses of gamma globulin might afford protection against virus B. According to this hypothesis, the two viruses would have a particular relationship to each other and this would result in some cross immunity. The validity of this hypothesis remains to be established.

In the present studies, large doses of gamma globulin were employed, in

order to ensure a clear-cut result. In a further series of experiments already in progress, the dose of gamma globulin has been reduced to half of that applied in the series at issue. The dose of gamma globulin required per kg body weight will probably be smaller for children and adults than that used with premature infants. The minimum dose for protection against hepatitis following transfusion remains to be determined in later experiments.

SUMMARY

In an experimental study of the prevention of transfusion hepatitis extending over a period of two years, 182 premature infants were given doses of 8 ml per kg body weight of a 10 per cent solution of gamma globulin, at the time of the first transfusion of blood or plasma. Two control groups were also set up, one of 205 infants receiving transfusions but no gamma globulin, and a second of 204 infants receiving neither transfusions nor gamma globulin. All groups

were treated identically in every other respect. In the group given transfusions and gamma globulin, only one case of hepatitis occurred, whereas in the group receiving transfusions but no gamma globulin, 15 contracted hepatitis. It seemed that by the administration of sufficiently large doses of gamma globulin, the incidence of transfusion hepatitis can be reduced, but further experiments are necessary before a definite standpoint can be taken.

LITERATURE

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