New Results in the Prevention of Transfusion Hepatitis

By

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Transfusion hepatitis may be prevented in two ways, (i) by selection of suitable, virus-free donors, and (ii) by protection with gamma globulin of the patient receiving the transfusion. As it has been shown previously, the first method cannot offer 100 per cent protection, there being no laboratory method by which the virus carriers could reliably be screened. Therefore the passive protection afforded by gamma globulin cannot be left unconsidered. As to the protective effect of gamma globulin, it is still generally believed that it affords protection exclusively against epidemic hepatitis but cannot prevent the development of transfusion hepatitis.

In a previous study [1] we started from the hypothesis that some cases of transfusion hepatitis might be caused by the A virus and in these high doses of gamma globulin would be effective, although it did not seem unlikely, either, that high doses of gamma globulin might afford some protection against the B virus.

The experiments were carried out on premature infants partly because they are given many transfusions of whole blood and plasma, and partly because their body weight being low, small quantities of gamma globulin are sufficient to ensure a high antibody level. Finally, in this case the mechanism of an eventual protection is easy to explain as in the absence of active antibody production only passive protection may play a part.

Thus we gave 8 ml/kg gamma globulin together with the first transfusion to about 50 per cent of the prematures involved in the investigations. While of the 205 controls, which had received transfusions without gamma globulin, 15 developed hepatitis (Table I, group 1), of the 182 of the transfusion + gamma globulin group only one contracted hepatitis (Table I, group 2).

In the group without gamma globulin there was 1 case of hepatitis for every 78 transfusions, in the gamma globulin-treated group this ratio was 1 to 964. No case of hepatitis occurred among a large number of simultaneously hospitalized prematures receiving neither transfusions nor gamma globulin. Accordingly, the infection was not oral, nor due to injections, but was transmitted by transfusion.

The results have proved that the incidence of hepatitis caused by blood or plasma transfusions could be reduced by the use of excessive doses of gamma globulin. The protective action may be explained in two ways.

Materials and Methods

Every premature infant receiving transfusions of blood and/or plasma was given simultaneously with the first transfusion or a few days after it 4.0 ml/kg body weight of gamma globulin intramuscularly. Prematures subjected to exchange transfusion were exceptions to this rule; in these cases the dose was 8.0 ml/kg. The group of prematures treated with transfusions but no gamma globulin in the previous experiment served as control, while the group receiving neither transfusions nor gamma globulin served for excluding the possibility of the occurrence of epidemic hepatitis. Blood was obtained from the National Blood Donor service. Most of the plasma originated from one donor, a small part was pooled plasma. Gamma globulin was supplied by the Institute for Serobacteriological Production and Research "Human", Budapest, and had a protein concentration of 10 per cent.

The experimental period lasted from December 1, 1961, till February 15, 1963.

Table I

Group	Number of cases	Transfusions per one premature infant		Number of cases of hepatitis	Number of transfusions per case of hepatitis
		Number (average)	Total, ml (average)		
Group 1. Transfusion only	205	5.7	102	15	78
Group 2. Transfusion + 8.0 ml/kg gamma globulin	182	5.3	82	1	964
Group 3. Transfusion + 4.0 ml/kg gamma globulin	423	7.0	147	3	987

(i) A certain percentage of the cases of transfusion hepatitis is caused by the A virus, against which gamma globulin affords protection. (ii) Excessive doses of gamma globulin may offer some protection against the B virus, too, owing to its antigenic component common with A virus.

In everyday practice it would be too expensive to use such high doses of gamma globulin as were applied in our first experiments made in order to elucidate certain basis principles. In the present studies we have therefore examined the incidence of hepatitis among premature infants treated with transfusions of blood or plasma and a dose of gamma globulin half of that mentioned above.

Results

During the mentioned period, 1030 premature infants were treated at the Hospital for Premature Infants. Of these 316 died, most of them a few days after birth. Of the survivors, 423 received transfusions and gamma globulin; 291 premature infants received neither transfusions nor gamma globulin. In the latter group no hepatitis occurred. In addition, 28 prematures were treated by blood exchange transfusion. None of these prematures developed hepatitis, but this group was too small to be evaluated separately. All infants had the same medical care and nursing.

About 50 per cent of the prematures had transfusions of blood, the rest transfusions of both blood and plasma. The number of blood and plasma transfusions was 2994, thus the average for 1 premature infant was 7.0; the average volume, 147 ml. The average interval between the injection of gamma globulin and the last transfusion was 37 days. Following the injection of gamma globulin, the transfusion series was discontinued after 40 days in about 50 per cent, and after 70 days in 90 per cent of the cases.

Of the 423 premature infants treated with transfusions and gamma globulin (4.0 ml/kg) 3 developed hepatitis (Table I, Group 3).

Case 1. B. E., received a total of 350 ml of blood and plasma on 20 occasions during the 2 1/2 months following birth. From all batches of plasma given to this baby, other infants, too, received transfusions. Of the bloods transfused to this baby, 21 others also received transfusions, 14 infants once, 4 twice and one infant 12 times. None of these infants developed hepatitis. The interval between the first transfusion and the onset of hepatitis was 87 days, that between the last transfusion and the onset of hepatitis was 18 days. The virus-containing blood must have therefore been among the first transfusions given to the baby. The baby recovered.

Case 2. S. P., received a total of 21 3 ml of blood and plasma on 14 occasions during the 45 days following birth. This infant received one batch of blood by himself, all the others he shared with other infants; the blood transfused to him were shared once with 12 other infants and twice with 1 infant. None of the other infants developed hepatitis. The interval between the first transfusion and the onset of hepatitis was 39 days. The patient recovered.

Case 3. H. R., a total of 285 ml of blood or plasma was administered on 24 occasions over 3 months following birth. Four blood specimens were given to this premature infant alone, the others were shared with 17 babies once, 5 twice, with 1 four times and with 1 five times. None of these other infants contracted hepatitis. The onset of hepatitis was noted on the 94th day after the first, the 20th day after the last transfusion. The patient recovered.

Summing up, the three babies were given transfusions on 58 occasions; of these in 53 instances the bloods and plasmas were shared with other infants.

Comparison of these results with those for the earlier groups receiving 8 ml/kg gamma globulin and those given no gamma globulin (Table I) revealed that gamma globulin in a dose of 4 ml/kg also definitely reduced the incidence of transfusion hepatitis.

Considering the number of premature infants, the incidence of transfusion hepatitis seems to have been higher among those treated with the lower dose of gamma globulin. However, if the number of transfusions is taken into account — and from the point of view of potential infection this was the more important factor —, the protective effect was the same in both groups.

Discussion

When evaluating the results the first question is whether epidemic hepatitis did not occur in the ward, as in that case the protection afforded by gamma globulin might be ascribed to its well-known effect against the A virus. As neither in the earlier nor in the present series of experiments was hepatitis observed in any of the premature infants who had no transfusions and had been given no gamma globulin, it may be stated that epidemic hepatitis did not occur in our material. The manipulations and injections other than those involved in the transfusions cannot be blamed, either, because there was no difference in this respect between the various groups. It is therefore certain that the hepatitis was mediated by transfusion in every case.

An objection that might be raised against the effectiveness of gamma globulin is that it might have been only the prematures developing hepatitis who had received blood preparations containing virus. However, in the previous experimental series the incidence of transfusion hepatitis in the group receiving no gamma globulin was comparable to the world-wide frequency of virus carriers. In the present series round 3000 transfusions of blood or plasma were performed, representing 3000 instances of potential infection, even if more than one infant was treated with the same preparation. We are unable to determine the exact number of the donors, since a number of infants was treated with the pooled plasma of from 5 to 10 persons, and because both the blood and plasma donors donated blood or plasma repeatedly.

It is unlikely that exclusively those 5 bloods or plasmas would have contained virus of which the affected prematures alone received transfusions. As it has been pointed out, in the first case there was no such preparation, which would have been given only to the infected infants. In the second case there was just one preparation, in the third there were 4, which the infants received alone. On 53 occasions they had shared the preparations with other infants, of which none developed hepatitis.

A comparison of the present results with those obtained in the previous series for the group treated with transfusions but no gamma globulin seems to prove that protection against transfusion hepatitis is afforded not only by 8.0 ml/kg, but also a 4.0 ml/kg dose of gamma globulin.

Summary

In previous experiments it was found that the incidence of transfusion hepatitis was significantly reduced among premature infants subjected to a series of blood or plasma transfusions when simultaneously with the first transfusion a high dose (8.0 ml/kg) of gamma globulin had been administered.

In the present experiments the dose of gamma globulin was reduced to 4.0 ml/kg, to determine how this would affect the incidence of transfusion hepatitis among premature infants. Of the 423 prematures thus treated 3 developed hepatitis.

By comparing this result with that obtained in the previous study, it may be stated that this lower dose of gamma globulin seemed to afford protection against transfusion hepatitis.

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Reference

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