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THE ROLE OF SURGERY IN TRANSMITTING « POST-TRANSFUSION HEPATITIS »

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Key words: Post-transfusion hepatitis - Post-surgery hepatitis - Analysis risk factors.

The role of surgery as an additional risk in transmitting « post-transfusion» hepatitis was investigated in a retrospective study on acute hepatitis occurring in 77 transfused patients, 293 transfused and operated patients and 243 hepatitis cases with history of surgery without transfusion.

Hepatitis A patients admitted to the same centres in the same period were utilized as controls. In transfused patients the percentage of NANB hepatitis was higher than that of type B (61.0% vs. 36.4%), while in the operated not transfused group the percentage of type B was twice that of type NANB (63.4% vs. 32.5%).

In transfused and operated cases intermediate values were observed. The age-adjusted measures of association between exposures and the different hepatitis types showed a lack of effect of transfusion and a dominant role of surgery in transmitting type B hepatitis. In contrast, NANB « post-transfusional » cases were actually a mixture of post-transfusional and post-surgical cases, since both these exposures were found to be significantly associated with the disease.

Our results suggest that studies on the incidence and the etiology of post-transfusion hepatitis should take into account the risk of surgical exposure which might have occurred.

INTRODUCTION

Post-transfusion hepatitis (PTH) is by definition an episode of acute viral hepatitis occurring 2-26 weeks after blood transfusion (1). However, an episode of acute viral hepatitis « after » transfusion may not necessarily be « caused by » transfusion (2). The majority of studies on PTH are usually done on patients receiving blood transfusion during surgery (3, 4, 11,12) and surgery may represent a risk factor in the acquiring of viral hepatitis (2). In addition, hepatitis acquired either through surgery or transfusion may show different etiological patterns.

Accordingly, we performed this retrospective study to elucidate the role of surgery as an additional risk in « post-transfusion hepatitis » and to evaluate whether the etiology of viral hepatitis in transfused patients varies or not in relation to exposure to surgical procedure.

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MATERIALS AND METHODS

We examined all cases of acute viral hepatitis admitted to 53 hospitals for infectious diseases throughout Italy during 1982 (6). Type A and B hepatitis were diagnosed by standard immunological methods; NANB hepatitis was diagnosed by exclusion of types A and B hepatitis and cytomegalovirus and Epstein-Barr virus infections also.

We excluded from the study politransfused and haemodialysis patients. Data of patients under 16 were not analyzed because of the negligible number of transfused patients in this age group; nor were data of Cytomegalovirus and Epstein-Barr virus hepatitis cases, which represented less than 1.5% of the PTH cases. Following these criteria, we studied 6653 patients, i.e. 975 affected by type A hepatitis, 4343 by type B and 1335 type NANB.

Considering previous exposures to blood transfusion and/or surgery during the 2-26 weeks preceeding the onset of the illness we recognized the following categories of patients:

Transfused patients (TP) - patients who received a blood transfusion not undergoing surgery (77 cases).

Transfused and operated patients (TOP) - patients who received blood transfusion and underwent surgery (293 cases).

Operated patients (OP) - patients with history of surgery without transfusion (243 cases).

The remaining 6040 patients had no history of transfusion or of surgery.

Age-adjusted measures of association between exposures and diseases were determined using overall odds ratio (OR) according to Woolf (5), standardized morbidity ratio (SMR) and directly standardized risk ratio (SRR) according to Miettinen (9).

Type A hepatitis cases served as a reference group.

OR is an estimate of the adjusted odds ratio obtained by combining the logarithms of odds ratio over strata; this is an adequate method when the number of strata is small or moderate and the homogeneity assumption is met (i.e. when odds ratio is assumed to be the same at each stratum of the confounding factor).

SMR is an estimate of the standardized risk ratio, with the exposed group as the standard, and may be interpreted as an estimate of the proportionate risk increase due to exposure among the unexposed; it does not require any homogeneity assumption (7). We calculated both OR and SMR, to check if the two estimates coincided.

SRR is an estimate of the standardized risk ratio with the non-exposed group as the standard (i.e. using the proportionate distribution of the stratification factor among the unexposed as the standard distribution). Thus, SRR for various categories of exposure are mutually comparable (8). SRR is an estimate of the proportionate risk increase that would be expected to occur among the unexposed if they had been exposed.

Additive effect for joint exposure was evaluated by the formula:

$$(SRR_{TOP}\text{-}1) = (SRR_{OP}\text{-}1) + (SRR_{TP}\text{-}1)\ (10).$$

In order to account for empty cells, stratum-specific odds ratios and their variances were calculated adding 0.5 to the cell frequencies (5).

RESULTS

History of blood transfusion was reported in 370 patients of the 6653 cases (5.56%); the percentage of transfused patients according to the age and to the etiology of hepatitis is reported in Table 1.

History of blood transfusion was present in 0.9% of type A, 3.4% of type B and 16.0% of type NANB hepatitis cases. As expected, the proportions of PTH increased with increasing age.

The age-adjusted OR are significantly higher than unity for both type B and type NANB hepatitis, 2.9 and 14.0 respectively.

To evaluate whether the etiology of acute viral hepatitis in transfused patients can vary or not

TABLE 1.

History of blood transfusion among 6653 type A, B and NANB acute viral hepatitis patients according to age. Absolute numbers and percentages (into brackets) are given.

	Age groups (years)			All cases	Age-adjusted odds ratio** (95% confidence limits)
	16-30	31-50	>50		
Type A	3/693 (0.4)	4/224 (1.8)	2/58 (3.4)	9/975* (0.9)	
Type B	29/3217 (0.9)	40/703 (5.7)	78/423 (18.4)	147/4343 (3.4)	2.9 (1.5-5.5)
Type NANB	36/794 (4.5)	76/270 (28.1)	192/271 (37.6)	214/1335 (16.0)	14.0 (7.4-26.4)

* 7 out of the 9 cases of type A PTH occurred whitin 2-8 weeks after transfusion.

** Calculated using type A hepatitis cases as a reference group.

with exposure to surgery, we studied the proportions of type A, B, and NANB hepatitis in transfused patients, transfused and operated patients and operated patients (Table 2). In transfused patients the percentage of NANB hepatitis is clearly higher than type B hepatitis (61.0 and 36.4% respectively). In contrast, in operated patients type B hepatitis has a percentage of almost twice that of NANB hepatitis (63.4 vs. 32.5%). In transfused operated patients the proportion of type B (40.6%) and NANB (57.0%) hepatitis were between those observed in TP and OP groups.

The role of transfusion and of surgery as a risk factor of acquiring type B and type NANB hepatitis was evaluated by calculating OR, SMR and SRR for the different categories of exposure (Table 3).

For type B hepatitis the age-adjusted OR in the TP group is not significantly different from unity, whereas it is statistically significant for TOP and OP groups (3.2 and 3.3, respectively). SMR results coincide with the OR estimates.

The SRR values confirm the absence of effects after transfusion and the dominant role of surgery in determining type B hepatitis, since SRR values were similar in the TOP and OP groups (3.59 and 3.41, respectively).

For type NANB hepatitis, the age-adjusted OR and the SMR are statistically significant for all three exposed categories. Comparison among the three groups after the SRR calculation indicates that the risk after transfusion alone (11.88) is greater than that after surgery alone (5.62). In TOP the value of SRR indicates an additive effect of the two exposures.

TABLE 2. — Percentages of type A, B and NANB hepatitis in transfused patients, transfused and operated patients and in operated patients, according to age groups.

Age groups (years)	Transfused patients			Transfused operated patients			Operated patients		
	Type A No. (%)	Type B No. (%)	Type NANB No. (%)	Type A No. (%)	Type B No. (%)	Type NANB No. (%)	Type A No. (%)	Type B No. (%)	Type NANB No. (%)
16-30	2(11.1)	6(33.3)	10(55.6)	1(2.0)	23(46.0)	26(52.0)	4(4.2)	71(73.9)	21(21.9)
31-50	0	6(27.3)	16(72.7)	4(4.1)	34(34.7)	60(61.2)	4(4.9)	42(51.2)	36(43.9)
>50	0	16(43.2)	21(56.8)	2(1.4)	62(42.7)	81(55.9)	1(1.5)	42(64.6)	22(33.9)
Total	2(2.6)	28(36.4)	47(61.0)	7(2.4)	119(40.6)	167(57.0)	9(3.7)	155(63.8)	79(32.5)

TABLE 3. — Age adjusted measures of association between exposure category and type of hepatitis. Type A hepatitis cases were used as a reference group.

Hepatitis (no. of cases)	Exposures categories (no. of cases)	OR[a] (95% confidence limits)	SMR[b] (95% confidence limits)	SRR[c]
Type B (4343)	Transfused (TP) (28)	1.2 (0.4-4.0)	1.9 (0.3-11.2)	1.59
	Operated (OP) (155)	3.2 (1.7-6.0)	3.8 (1.9-7.4)	3.59
	Transfused operated (TOP) (119)	3.3 (1.6-6.7)	3.6 (1.6-8.0)	3.41
Type NANB (1335)	Transfused (TP) (47)	7.8 (2.4-22.8)	11.2 (2.2-55.9)	11.88
	Operated (OP) (79)	6.8 (3.5-13.2)	6.7 (3.3-13.5)	5.62
	Transfused operated (TOP) (167)	16.0 (7.9-32.3)	14.6 (6.8-31.3)	16.15

[a]OR = overall odds ratio.
[b]SMR = standardized morbidity ratio.
[c]SRR = directy standardized risk ratio.

DISCUSSION

The reported data indicate that type B hepatitis occurring after blood transfusion may be the consequence of a concomitant surgical procedure rather than of the transfusion alone.

In contrast, « post transfusional » NANB hepatitis is actually a mixture of post-transfusional and post-surgical cases, since both these exposures were found to be significantly associated with the disease and to act in an additive manner to transmit NANB hepatitis. In our series surgical exposure was present in about 80% of NANB PTH.

Our data were drawn from a case-control study performed on 6653 cases selected from a large series of patients representing about one-third of all reported cases during 1982 in Italy (6).

Type B and NANB hepatitis patients were « cases » and type A hepatitis patients were utilized as a reference group. This procedure allowed us to reduce the recall bias. In fact, in our patients exposure information was collected on admission to hospital when the etiological diagnosis was not yet known. In estimating the odds ratios, we assumed that exposures were not related to AVH. If a positive association was present (in literature only reported in rare circumstances), the odds ratios relative to type B and NANB hepatitis would be slightly underestimated.

Finding that surgery is strongly associated with B and NANB hepatitis the problem of what means of transmission are involved may raise. In theory, we may presume the presence of unknown carriers of hepatitis viruses among hospital personnel, unsatisfactory methods of sterilizing surgical instruments, or other possible transmission routes occurring during hospitalization. It must be stressed that our data have been collected in a geographical area in which hepatitis B is particularly endemic and therefore the association between hepatitis B and surgery which we found could reflect this epidemiological situation. In fact, in a HBV low endemicity area such as USA, Aach et al. (2) found only cases of NANB hepatitis among hospitalized patients, who for the most part had undergone surgery without transfusion.

In the series studied by us joint exposure to transfusion and surgery was recorded in about 80% of all the PTH cases. According to the addivity effects of the exposure (Table 3), in our PTH cases not less than one-third must be due to surgery rather than transfusion alone. Therefore, as the majority of studies on the incidence and etiology of PTH are performed in transfused and operated patients, the transfusional risk has possibly been overestimated since the surgery risk was not taken into account.

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