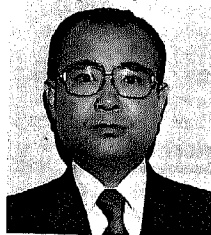


Vitamin C for Prophylaxis of Viral Hepatitis B in Transfused Patients

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Fukumi Morishige was born in Fukuoka, Japan, on October 24, 1925. He received his M.D. degree in 1961 from Kurume University School of Medicine. Since 1967 he has been chief surgeon of Fukuoka Torikai Hospital. To prevent serum hepatitis in blood transfused patients he has administered large doses of vitamin C. He is a Non-resident Fellow of Linus Pauling Institute.



Akira Murata was born in Shimonoseki on August 2, 1935. He received his Ph.D. degree in microbiology in 1964 from Kyushu University. Since 1966 he has been an Associate Professor at Saga University. He has investigated the virucidal effect of vitamin C. He studied at Linus Pauling Institute in 1976 and 1978.

They have collaborated in studies of vitamin C in relation to viral diseases and presented both the laboratory studies and the clinical observations at the First Intersectional Congress of the International Association of Microbiological Societies held in Tokyo in September 1974.

Introduction

We reported in 1975 the clinical observation in the years 1967 to 1973 that the incidence of post-transfusion hepatitis was remarkably reduced by large doses of vitamin C (ascorbic acid, sodium ascorbate) (Morishige & Murata, 1975, 1976).

New Findings

This paper describes the results of this clinical trial, now extended to 1976. The trial was conducted at the Fukuoka Torikai Hospital, a 220-bed general hospital in Japan, which was opened in August 1967. In the trial many of the patients received large doses (2 to 6 g or more per day) of vitamin C after whole blood transfusion.

The director of the hospital, Morishige, had observed in 1955 that the administration of vitamin C appeared to reduce the incidence of post-transfusion hepatitis in patients in the Fukuoka Tachiarai Hospital. This observation led to the earlier trial, 1967 to 1973, which has now been extended to 1976.

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We believe that the assignment of patients to the low-C and high-C groups was essentially random, although no formal randomization process was carried out. The fraction in the low-C group decreased from about 15% in the early years to nearly zero in 1976.

Table 1 shows the annual incidence of post-transfusion hepatitis in 1974 to 1976. During the three years there were four cases of hepatitis among the 292 transfused patients. A summary of the hepatitis cases, including the dosages of vitamin C, is shown in Table 2. There was one case of hepatitis B, but the patient (case 12) had received only small doses (1 g or less per day) of vitamin C and received no vitamin C for eight weeks before the onset of hepatitis. The three hepatitis patients who had received large doses of vitamin C showed no evidence of

Table 1
Incidence of post-transfusion hepatitis
at Fukuoka Torikai Hospital

Year	Number of patients transfused ^a	Post-transfusion hepatitis			Attack rate(%)
		Number of cases			
		Type B	Type non-B	Total	
1974	108	1 ^b	1	2	1.85
1975	87	0	0	0	0
1976	97	0	2	2 ^c	2.06
Total	292	1	3	4	1.37

Patients received whole blood from the Fukuoka Red Cross Blood Center. The transfused patients were followed biweekly to monthly for six months. Patients developing elevations of SGPT were followed more frequently. The diagnosis of hepatitis was a result of Yoshitoshi's criteria in which a SGPT level of greater than 200 units was used. Laboratory tests included also SGOT, total bilirubin, icteric index, alkaline phosphatase, γ -GTP, HBsAg and anti-HBs. Patients received no immune globulin.

^a Excludes patients with no follow-up.

^b The patient received small doses (1 g or less/day) of vitamin C after the transfusion.

^c There was another case of hepatitis with peak SGPT level of 180. Tests for HBsAg and anti-HBs were negative.

Table 2
Summary of post-transfusion hepatitis cases

	Case No.			
	12 ^a	13	14	15
Initials	T.A.	T.D.	M.K.	F.I.
Age	46	72	34	59
Sex	M	M	F	F
Primary disease	Cerebral hemorrhage, Renal insufficiency	Pulmonary emphysema and carcinoma	Uterine atonic bleeding	Pulmonary carcinoma
Transfusion Year	1974	1974	1976	1976
Total amounts of blood	800	1000	1000	1200
Frequency	4	1	1	2
Hepatitis Incubation period (week)	16	2	4	6
Peak SGPT value	1440	650	900	651
Peak SGOT value	1140	550	728	471
Peak alkaline phosphatase value	12.9		15.8	52
Peak icteric index value	30	9	20	36
Duration of elevated SGPT value (week)	1 ^b	3 ^c	6	11
HBSAg ^d Before ^e	-	-	-	-
During ^f	+	-	-	-
Anti-HBS Before ^g			+	+
During ^f			+	+
Vitamin C ^g (average g/day)				
Week 1	0.3	3.7	6.3	6.3
2	0.4	3.0	6.0	11.1
3	1.0		2.6	6.0
4	1.0		0	6.0
5	1.0			7.4
6	1.0			8.0
7-8	0.7			
9-16	0			

^a Case Nos. 1 to 11 appeared in our previous paper (Morishige & Murata, 1976).

^b Died of respiratory infection with renal failure during the treatment on 124th day after the first transfusion.

^c Died of postoperative pulmonary insufficiency during the treatment on 38th day after the transfusion.

^d Tested by radioimmunoassay.

^e Before the transfusion.

^f During hepatitis.

^g Dose and given periods between the first transfusion and the onset of hepatitis. After that therapeutical dose of vitamin C was given for treating the cases.

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hepatitis B as judged by the negative detection of HBs antigen by radioimmunoassay, which is much more sensitive than other methods in the detection of HBs antigen. Patient 13, whose abnormal SGPT value was highest at the second week, with subsequent decline, was presumed to have drug-induced hepatitis. Patients 14 and 15, being carriers of hepatitis B antibody, were presumed to have type non-A, non-B hepatitis.

There were very few control patients during the years 1974 to 1976 because by 1974 the value of ascorbic acid had become so clear that the decision was made, for ethical reasons, to give vitamin C in large amounts to essentially every patient. During the period 1967 to 1973, there were 150 patients who were given blood transfusions and who received little or no vitamin C (less than 2 g per day). Of these patients, 11 developed hepatitis (seven percent), as reported in the earlier paper, where it was reported also that among 1,100 similar transfused patients who received 2 g or more of vitamin C per day there were no established cases of hepatitis and only a few questionable cases.

Conclusion

Over the whole period 1967 to 1976 there were 12 cases of hepatitis among the 170 transfused patients who received little or no vitamin C (incidence 7%) and three cases, all non-B, among the 1,367 who received 2 g per day or more (incidence 0.2%).

The results presented here support our earlier conclusion that vitamin C given in large amounts has a significant prophylactic effect against post-transfusion hepatitis, especially type B.

Summary

An earlier study, 1967-1973, showing that the incidence of post-transfusion hepatitis is remarkably reduced by large doses of vitamin C has been continued in Fukuoka Torikai Hospital during the years 1974 to 1976. Large doses, two grams or more per day, of vitamin C after whole blood transfusion were administered to 272 transfused patients. Only three cases of hepatitis (all non-B) were observed. Between 1967 and 1976 there have been in this hospital no hepatitis-B cases among a total of 1,367 patients who received large doses of vitamin C after blood transfusion. The incidence of hepatitis in transfused patients was 7% for those who received little or no vitamin C and 0.2% for those who received 2 g per day or more.

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F. Morishige and A. Murata

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