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Editorial

Should people with hepatitis C virus infection receive a bone marrow transplant?

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Recently, several studies in this journal and elsewhere have discussed the impact of hepatitis C virus (HCV) infection on the outcome of bone marrow transplants.[1–18] This is an important issue because of the high frequency of HCV infection, mostly from prior transfusions, in potential transplant recipients. Case reports of post-transplant liver failure in people with prior non-A non-B (NANB) presumably HCV hepatitis, warned about potential risks. Also, several studies suggested that the transplant-associated immune suppression may alter NANB hepatitis virus infection.[19–21] However, a critical evaluation of the impact of prior HCV infection on transplant outcome is difficult because of the many differences in the incidence of HCV infection, the tests to detect HCV infection,[22] the distribution of HCV genotypes in infected populations,[16,23] the transplant strategies, and the diagnostic criteria for acute and chronic hepatitis and/or for liver failure.[12,13] For example, definitive diagnosis of HCV infection in immune compromised subjects receiving transfusions requires detection of HCV RNA;[8,11,21,22,24,25] this is rarely tested in transplant studies. The conclusion is that it is difficult to known which subjects have HCV infection. Another problem is ascribing post-transplant liver function abnormalities to HCV infection *vs* (or combined with) other causes of liver failure including drugs, radiation toxicity, acute and chronic graft-versus-host disease (GVHD), and infections from other hepatotropic viruses (such as cytomegalovirus (CMV) or other infectious agents).

Table 1 summarizes data on the impact of HCV infection in bone marrow transplant recipients in seven studies. These studies were chosen because they compared post-transplant liver abnormalities in subjects with and without HCV infection. Controls in most of these studies are not truly comparable, differing in surveillance for hepatitis, liver function test abnormalities and other endpoints.

Abnormal post-transplant liver function tests were reported in 85% (95% confidence interval, 78–92%) of subjects with HCV infection pretransplant *vs* 59% (51–67%, $P = 0.0001$) in subjects without HCV infection pretransplant. This difference may reflect persisting abnormal pretransplant liver function, increased hepatic damage in HCV-infected subjects and/or ascertainment biases. For example, it is likely that people with prior hepatitis may have more frequent liver function tests than others.

Hepatic veno-occlusive disease (VOD) was reported in 14% (4–24%) of subjects with, *vs* 8% (6–10%, $P = 0.2$) of subjects without, pretransplant HCV infection. It should be noted that most HCV-infected subjects with VOD originate from one single series.[16] Liver failure occurred in 12% (1–23%) of subjects with HCV infection *vs* 11% (7–15%, $P = 0.6$) of subjects without pretransplant HCV infection.

Another issue is whether a transplant increases the likelihood of progression to chronic hepatitis in people with pretransplant HCV-infection. Chronic hepatitis was reported in 59% (48–70%) of subjects with pretransplant HCV infection *vs* 29% (24–34%, $P < 0.0001$) of subjects without pretransplant HCV infection. This 59% incidence of chronic hepatitis is similar to the 50 to 70% incidence of chronic hepatitis in people with HCV infection not receiving a bone marrow transplant.[26,27]

The follow-up of the published studies is inadequate to assess the long-term impact of HCV infection. However, since HCV infection does not adversely effect the survival of people with community acquired infection,[28] it is unlikely it would effect the long-term survival of those that have undergone a bone marrow transplant.

In summary, although people with pretransplant HCV infection have a greater risk of having abnormal liver function tests and developing chronic hepatitis than those without HCV infection pretransplant, these risks are similar to those in HCV-infected individuals without a bone marrow transplant. Also, the high risk of chronic hepatitis should be viewed in the context of the disease for which the transplant is being considered, for example, an otherwise incurable disease like recurrent acute lymphocytic or acute myelogenous leukemia. Should people with pretransplant HCV infection receive a bone marrow transplant? Yes, if they need it, but caution is required. Although there are no data showing that different conditioning or GVHD prevention regimens increase the risk of liver damage, it may be wise to avoid drugs such as busulfan or methotrexate that can damage the liver.

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Table 1 Liver abnormalities in BMT recipients with and without pretransplant HCV infection

Ref.	*Method of HCV detection*	*Abnormal liver function tests*		*Veno-occlusive disease*		*Liver failure*		*Chronic hepatitis*	
		HCV+	*HCV–*	*HCV+*	*HCV–*	*HCV+*	*HCV–*	*HCV+*	*HCV–*
14	1st G ELISA	7/10	22/25	0/10	1/25	1/10	2/25	—	—
5	HCV-RNA	8/11	2/8	0/11	1/8	2/11	1/8	—	—
15	2nd G ELISA 2nd G RIBA	—	—	1/7	11/167	1/7	19/167	6/7	53/167
16	HCV-RNA	—	—	5/6	9/52	—	—	—	—
9	2nd G ELISA	40/45	17/28	—	—	—	—	23/49	10/44
6	2nd G ELISA	5/5	17/24	0/5	0/24	0/5	3/24	5/5	11/24
17	2nd G ELISA	17/20	32/68	—	—	—		14/20[a]	15/68
18	HCV-RNA	—	—	1/10	13/161	—	—	—	—
Total (%)		77/91 (85)	90/153 (59)	7/49 (14)	35/437 (8)	4/33 (12)	25/224 (11)	48/81 (59)	89/303 (29)
P		0.0001		0.2		0.6		<0.0001	

[a]One patient developed liver cirrhosis.
[b]1st G ELISA: first generation ELISA.
[c]2nd G ELISA: second generation ELISA.
[d]RIBA: recombinant immunoblotting assay.

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