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Title:

IN THE ERA OF NUCLEIC ACID TESTING, IS PERMANENT DEFERRAL OF GAMETE DONORS WITH ISOLATED POSTIVE SEROLOGICAL RESULTS FOR HEPATITS STILL NECESSARY?

Authors:

S. Chang[1, 2]; C. Antonelli[3]; A.B. Copperman[1, 2]; J. Shamonki[3]

Affiliations

1. Reproductive Medicine Associates of New York, 635 Madison Avenue, 10th Floor New York, NY, United States, 10022
2. Department of OBGYN and Reproductive Science, Icahn School of Medicine at Mount Sinai, Klingenstein Pavilion, 9th Floor 1176 Fifth Ave. New York, NY, United States, 10029
3. California Cryobank, 11915 La Grange Avenue, Los Angeles, CA 90025

Objective:

The risk of transfusion and transplant-related Hepatitis B (HBV) and Hepatitis C (HCV) transmission has been steadily reduced through adoption of routine screening for Hepatitis B surface antigen (HBsAg), anti-Hepatitis B core antigen (anti-HBc), and anti-Hepatitis C. Despite their utility, these antibody-based assays are prone to false positive results, and due to inherent test sensitivity and/or dependence on host response, are also limited by a substantial window period between infection and detection. The more recently available nucleic acid testing (NAT), offers improved sensitivity and specificity over antibody-based assays, significantly decreasing the acute infection window period and improving detection of infections well into late chronic phases. Concurrent NAT testing is suspected to be useful for differentiating serological false

positive results from true infected potential donors. Blood transfusion literature has shown that 2-16% of donors that tested positive for HBsAg were in fact HBV DNA negative after NAT.[1] The aim of this study was to determine the true incidence of HBV and HCV in potential gamete donors, and evaluate if a re-entry protocol for suspected false positive results using concurrent NAT testing should be considered.

Design:

Retrospective, cohort study

Materials and Methods:

The study included 1396 gamete donors presenting at various donation sites between 2016 and 2018 and being screened for HBV and HCV. HBsAg, anti-HBc, HCV antibody, and triplex (HIV-1, HCV, HBV) NAT results were analyzed. Serologic and virologic results were compared. Charts of donors testing positive were reviewed manually for accuracy.

Results:

Of the 1041 sperm donors and 355 egg donors included in this study, 6 (0.58%) sperm donors and 4 egg donors (1.12%) were found to be positive for either HBsAg or anti-HBc (Table 1). Two of the sperm donors were found to have an active infection (positive HbsAg and Anti-HBc, confirmed on NAT). One egg donor was found to have immunity from natural infection (positive anti-HBc and anti-HBs, negative NAT). Three donors (2 sperm and 1 egg) were diagnosed with either a resolved infection or false positive (positive for Anti-HBc but negative for HbsAg and HBV NAT). Four donors (2 sperm, 2 egg) were found to have a false positive result (positive

HBsAg, but negative anti-HBc and NAT), yielding a 40% false positive rate in this cohort. Five sperm donors were found to have antibodies to HCV (0.48%) and were negative for HCV NAT (Table 2), suggesting a 100% false positive rate.

Conclusions:

This study demonstrated the true positive rate for HBV and HCV was low in the gamete donor population, whereas the false positive rate was substantial (at least 40% for HBV and 100% for HCV). Universal concurrent testing with NAT is currently recommended by FDA for blood and tissue donors. Experts suggest that a combination of Triplex NAT and anti-HBc testing is ideal, as it allows earlier detection of HBV infection, and captures individuals with chronic infections and low DNA levels. [2] Conversely, HBsAg testing has not been shown to provide additional information over NAT testing alone, and may ultimately become obsolete in donor screening programs. Given the currently lack of a re-entry protocol for presumed false positive testing results, current requirements for permanent deferral for any positive screening test result leads to unnecessary donor loss. While patient safety must always be prioritized, gamete donors are a scarce resource, and deferral based on spurious values creates issues for donor supply, particularly in cases where sibling pregnancies are desired. Particularly given the numerous opportunities for retesting a sperm donor within the 6 month quarantine period, a rigorous re-entry process for gamete donors, similar to that allowed for blood donors, should be considered. Accumulating data strongly suggests that HBsAg testing may add little, if any, HBV risk reduction value when HBV NAT and anti-HBc screening also apply.

Table 1:

Serologic results for the donors who screened positive for Hepatitis B

Source	HbsAg	Anti-HBc	Anti-HBs	IgM anti-HBC	HBV NAT	Interpretation
Sperm	Reactive	Reactive	N/A	N/A	Reactive	Infected
Sperm	Reactive	Reactive	N/A	Nonreactive	Reactive	Infected
Egg	Reactive	Reactive	Reactive	Nonreactive	Nonreactive	Immune 2/2 natural infection
Sperm	Nonreactive	Reactive	N/A	Nonreactive	Nonreactive	False positive vs. resolved infection
Sperm	Nonreactive	Reactive	N/A	Nonreactive	Nonreactive	False positive vs. resolved infection
Egg	Nonreactive	Reactive	N/A	Nonreactive	Nonreactive	False positive vs. resolved infection
Sperm	Reactive	Nonreactive	N/A	N/A	Nonreactive	False positive
Sperm	Reactive	Nonreactive	N/A	N/A	Nonreactive	False positive
Egg	Reactive	Nonreactive	N/A	N/A	Nonreactive	False positive
Egg	Reactive	Nonreactive	N/A	N/A	Nonreactive	False positive

Table 2: Serologic results for donors who screened positive for Hepatitis C

Source	Anti-HCc	HCV NAT	Interpretation
Sperm	Reactive	Nonreactive	False positive
Sperm	Reactive	Nonreactive	False positive
Sperm	Reactive	Nonreactive	False positive
Sperm	Reactive	Nonreactive	False positive
Sperm	Reactive	Nonreactive	False positive

References:

1. Niederhauser C. Reducing the risk of hepatitis B virus transfusion-transmitted infection. J Blood Med 2011; 2:91-102.
2. Stramer SL, Zou S, Notari EP, et al. Blood donation screening for hepatitis B virus markers in the era of nucleic acid testing: are all tests of value? Transfusion 2012; 52:440-446.