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State of the Art

Fifteen years of Nucleic Acid Testing in France: Results and lessons

Quinze ans de DGV en France : bilan et enseignements

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Abstract

Of the 40 million donations screened with Nucleic acid testing (NAT) between July 2001 and December 2015 in France, 20 HIV-positive, 13 HCV-positive and 17 HBV (HBV-NAT was initiated in 2005 and extended to the whole country in 2010) donations were discarded thanks to NAT. The main benefit in terms of discarded donations is related to HBV with a yield of 0.88 per million donations, which is 12.5 and 1.8 times higher than for HCV and HIV respectively. The main risk factor found in these donors during the post donation interview was having sex with men for males ($n = 11$, all repeat blood donors), having a partner HCV positive ($n = 6$) or at-risk partner (originated from endemic area or HBV positive) for HBV ($n = 8$) for HIV, HCV and HBV, respectively. Although the mean viral load was high for HIV (5.6 log copies/mL) and HCV (7 log IU/mL), HBV cases show low level of DNA (1.8 log IU/mL) demonstrating the need of a highly sensitive NAT assay. Overall, the clinical benefit for recipients remains those related to the prevention of HIV contaminations since HCV avoided transmissions are extremely rare (only one case in the last 5 years thanks to NAT) and the potential infectivity of HBV-NAT only positive cases is questionable due to the low level of HBV DNA and the presence of anti-HBs in more than a half of DNA positive/HBsAg and anti-HBc negative donors.

Keywords: NAT; HIV; VHC; VHB; France

Résumé

Parmi les 40 millions de dons de sang testés par dépistage génomique viral (DGV) entre juillet 2001 et décembre 2015 en France, 40 ont été écartés grâce au dépistage des génomes viraux (20 VIH, 13 VHC et 17 VHB, le DGV-VHB a été systématisé à la fin 2010 après une introduction progressive débutée en 2005 dans les territoires ultramarins et 2006 au CTSA). Le bénéfice le plus important s'est révélé être celui lié au dépistage du VHB avec un taux de 0,88 par million de dons, soit 12,5 et 1,8 fois plus que pour le VHC et le VIH, respectivement. Le facteur de risque principal retrouvé lors de l'entretien post-don était : pour les hommes, d'avoir eu des relations sexuelles avec d'autres hommes pour le VIH, ($n = 11$, tous étaient des donneurs connus), avoir un partenaire VHC positif ($n = 6$) pour le VHC et un partenaire à risque (originaire de zone d'endémie ou VHB positif) ($n = 8$) pour le VHB. Les charges virales étaient élevées pour le VIH (5,6 log copies/mL) et le VHC (7 log IU/mL), en revanche les cas VHB présentaient de faibles niveaux d'ADN circulant (1,8 log IU/mL) montrant l'intérêt d'utiliser des tests ultra-sensibles pour sa détection. Le bénéfice clinique pour les receveurs revient toutefois à la prévention de la transmission du VIH puisque les cas évités sont exceptionnels pour le VHC (un seul cas dans les 5 dernières années) et du fait que l'infectiosité des cas VHB reste hypothétique en raison des charges virales faibles et de la présence d'anticorps anti-HBs chez plus de la moitié des donneurs concernés.

Mots clés : DGV ; VIH ; HCV ; HBV ; France

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1. Introduction

Since the end of the nineties, Nucleic acid testing (NAT) has been progressively implemented in several high-income countries, at the beginning to avoid Hepatitis C virus (HCV) and Human Immunodeficiency virus type 1 (HIV-1) infections, and more recently to improve blood safety for Hepatitis B Virus (HBV). The main objective of the introduction of molecular diagnostic method in blood banks was to reduce the residual risk of viral contamination by transfusion due to the early phase of disease that was undetectable by classical serological assays. For HBV, it appears that another specific risk associated with extremely low viral DNA levels in blood donors with occult HBV infection (OBI) who are HBsAg negative could be prevented by NAT especially in the absence of anti-HBc antibodies against the HBV Core antigen (anti-HBc) testing [1].

An international survey [2] performed on the auspices of ISBT including 37 countries reporting results from NAT screening, showed that approximately 3000 viraemic donations would have been missed by serological screening methods among 300 million donations tested for HIV and HCV and over 100 million donations for HBV in a period ranging from 1998 to 2008. Subsequently, NAT screening conducted with multiplexed HIV/HCV/HBV assay performed on highly automated instrument platforms that ensuring reliable results, has easily been extended to other agents especially emergent pathogens.

In France, NAT has been introduced for all blood donations in 2001 for HCV and HIV-1[3], extended to HBV in 2005 in overseas territories, in 2006 in Army blood service and in the whole country in 2010. NAT for *arboviruses* has been temporary introduced to face specific outbreaks especially in overseas territories (Chikungunya, Zika) [4–6] as well as in 3 departments in the South of France in 2010 to prevent West Nile Virus transmission.

This paper presents the results and lessons of the fifteen first years of HIV-1/HCV/HBV NAT in France.

2. Method

NAT was initially introduced in some countries on the basis of "home-made" technologies due to the lack of standardized assays compatible with the high throughput imposed by blood banks organization. In France, the 10 first years of NAT were based on mini-pool (MP) testing with two methods: pools of 8 for approximately 40% of blood donations which were tested with Procleix HIV-1/HCV Assay from Gen-Probe/Chiron (Gen-Probe Inc., San Diego, CA; Chiron Corp., Emeryville, CA) and pools of 24 with Roche Cobas, AmpliScreen/Amplicor (Roche Dia gnostics GmbH, Mannheim, Germany) system for the remaining 60% [3]. In 2010, the Roche system was progressively abandoned and HBV-NAT was introduced. Since mid-2013, all donations have been individually tested with the triplex nucleic acid test, Procleix Ultrio Assay on the Tigris platform (Grifols, Meyreuil, France) [7] in mainland France and in Panther system (since 2014) in overseas territories. Fig. 1 shows the testing organization from 2001 to 2015. A supplemental testing including viral load determination (Cobas Taq Man assays Roche, limits of quantification 34 copies/mL, 25 IU/mL and 6 IU/mL for HIV, HCV and HBV, respectively) and genotype characterization [8,9] is performed at the National Reference Center, INTS to which a sample from each positive donation is sent to be used for further testing within the framework of the national surveillance of blood donor population [10].

3. Results

From the 1st July of 2001 to the 31st December of 2015, 40 million donations have been tested for HIV-1 and HCV-RNA and 16.5 million for HBV-DNA. Of the 486, 2798 and 1583 donors confirmed positive for HIV, HCV and HBV respectively, the number of NAT only positive (presence of nucleic acid and negative for the specific serology) cases was 22 (4.5%), 15 (0.5%) and 17 (anti-HBc negative) (1.1%) for HIV-1, HCV and HBV respectively.

The main characteristics of these donations are reported in Table 1 and the number of cases per year showed in Fig. 2.

4. HIV-NAT

Of the 22 HIV-1-NAT only positive cases, 18 were repeat blood donors (RBD) (median inter-donation delay 125 days excluding one donor with 1956 days), 20 were males (11 declared having had sex with men (MSM) during the post donation interview) and 2 females (with partner from endemic area, one from Guadeloupe, one from Africa); the mean viral load (VL) was 5.63 (1.6–6.5) log cps/mL (see VL distribution in Fig. 4), 15 were gtB, 3 gtC, 3 gtCRF02. Two donors of these 22 cases would have been discarded even without NAT due to the presence of another marker (one syphilis positive and one anti-HBc positive). Thus, at the end of 2015, the yield of HIV-NAT was 20.

Of the 486 HIV donors found positive in the study-period, 14 (2.9%) were anti-HIV positive/NAT negative: 6 were infected with HIV-2 and one with a HIV-1 group O which were undetectable with NAT assays used at that time, and 7 had too low viral loads to be detected by NAT performed in MP (none since 2008).

5. HCV-NAT

Of the 15 HCV-NAT only positive cases, 10 were repeat BD (median interdonation delay 379 days), 8 were males and 7 females, among those who were seen in post donation interview, 50% had a HCV positive partner; the mean viral load was 6.99 (1.39–7.7) log IU/mL (see distribution in Fig. 4), 8 were gt1a, 1 gt1b, 3 gt3a and 1gt4a. As two were positive for another marker (ALT, anti-HBc positive), the yield of HCV-NAT was 13.