Clinical Outcomes of Post-exposure Prophylaxis following Occupational Exposure to Human Immunodeficiency Virus at Dental Departments of Hiroshima University Hospital

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Abstract: Background: Dental professionals have so many opportunities to use injection needles and sharp instruments during dental treatment that they face an increased risk of needlestick injuries. This retrospective study reports the utilization and clinical outcomes of occupational post-exposure prophylaxis (PEP) with anti-retroviral agents after being potentially exposed to HIV at the dental departments of Hiroshima University Hospital.

Objective: This study reports the utilization and clinical outcomes of occupational post-exposure prophylaxis (PEP) with antiretroviral agents after being potentially exposed to HIV at dental departments of Hiroshima University Hospital.

Methods: Data on the clinical status of HIV-infected source patients and information on HIV-exposed dental professionals from 2007 to 2018 were collected.

Results: Five dentists with an average experience of 5.6 years (1-15 years) were exposed. The averaged CD4-positive cell number and HIV-RNA load were 1176 (768-1898) /μl and less than 20 copies/ml, respectively, in all the patients. Two of the five HIV exposed dentists received PEP. Three months after the exposures, all of their results were negative in HIV antibody/antigen tests.

Conclusion: These data might support the concept of “undetectable equals untransmittable”, although HIV exposure in this study was not through sexual transmission.

Keywords: HIV, U=U, occupational exposures, post-exposure prophylaxis, needlestick injury, dental treatment.

1. INTRODUCTION

Dental treatments often involve the use of sharp instruments that result in bleeding (e.g., pulpectomy, tooth extraction, scaling, root planing, dental local anesthesia, etc.) [1-4]. Thus, there is an increased risk to the dentists of occupational blood-exposure by needlestick injuries [5-9].

An Australian group showed that 27.7% of dentists experienced needlestick injuries in one year [10]. According to the questionnaire replies from 97 dental care workers working at dental clinics in Sumida City, Tokyo, Japan, 70.3% of the dentists and 77.2% of the dental hygienists and dental assistants were exposed to needlestick injuries [11]. Another questionnaire survey was conducted targeting 167 dentists and 152 co-dentals who work at dental clinics in Gifu Prefecture, and 84% of the dentists and 72% of the co-dentals experienced needle stick injuries during the respondents’ lifetime [12]. The most common causative devices were needles and burs during dental treatment or cleaning up [10, 13].

Previous data on the probability of HIV transmission by hollow needlesticks showed that the average risk rates of HIV-transmission after percutaneous exposure to HIV-infected blood and after mucus membrane exposure are approximately 0.3% and 0.09%, respectively [14-16]. Thus, HIV infectivity by this method is low [17]. In recent years, the U = U (Undetectable=Untransmittable) campaign has been launched worldwide by the Prevention Access Campaign [18-20]. The U = U is a simple but very important campaign based on scientific evidence. In 2008, a Swiss Statement showed that HIV-positive individuals whose viral load had been suppressed for at least 6 months with effective anti-retroviral therapy (ART) did not sexually transmit HIV [21]. In addition, large international studies have shown that...
HIV-positive individuals whose viral load is continuously below the detection limit do not transmit HIV to their partners despite condomless sex [22-24]. There are several other reports that provide scientific evidence [24-27].

None of the antiretroviral agents has received FDA approval for the post-exposure prophylaxis (PEP) of HIV [28-31]. However, the rationale for offering PEP for HIV is based on studies of the efficacy of antiretroviral chemoprophylaxis in animal models and on a case-control study [32-34]. The United States Public Health Service (US PHS) recommend PEP for persons with occupational exposure to HIV and the use of a full 4-week anti-retroviral regimen [35].

However, there is no report on the utilization and clinical outcomes of PEP after dental-occupational exposure to HIV at dental clinics. In this study, we have experienced and reported the utilization and clinical outcomes of PEP among dental staff after being potentially exposed to HIV during dental treatment at Hiroshima University Hospital.

### 2. METHODS

Cases of accidental occupational exposure to HIV that had occurred in the dental departments of Hiroshima University Hospital between 2007 and 2018 were experienced. Approval for this study was obtained from the research ethics board of Hiroshima University (approval number: epidemiology - 1485).

For exposed dental professionals, their profession, years of clinical experience, injury-causing instrument, adherence of blood to the offending instrument, taking PEP for HIV and its regimen, adverse effects, and occupational transmission were investigated. For source patients, their number of CD4-positive cells, plasma HIV viral load and period of undetectable HIV viral load were examined. It is standard to measure VL once every 2-3 months. However, in some patients, it is measured once a month. Fourth-generation HIV Ag/Ab combination immunoassays (ESPLINE HIV Ag/Ab; Fujirebio Inc., Tokyo, Japan) were used to monitor for HIV seroconversion after occupational exposure [36-40]. After baseline examination at the time of exposure, follow-up testing was performed at 4 weeks and 12 weeks after the exposure.

### 3. RESULTS

Evaluation of the records of patients who underwent dental procedures during a 10-year investigation period revealed five potential occupational exposures to HIV. All the exposed persons were dentists (Table 1). The mean experience of the dentists (range; minimum to maximum) was 5.6 years (1-15 years) (Table 1). The five source patients had a mean CD4-positive cell count (range; minimum to maximum) of 1176 (768-1898 /μl), and four of them had had <20 copies/ml (undetectable HIV viral load) for more than 6 months before the dental treatment (Table 1). Injury-causing instruments in four of the dentists were a diamond bur, a dental explorer, scissors and an injection needle, respectively (Table 1). A patient’s central incisor also led to an injury in one dentist. Her finger was injured by the incisal edge of the maxillary central incisor while making an impression of the patient’s mandibular teeth (Table 1). In two cases, blood was visibly adherent to the injury-causing instruments (Table 1). After their exposure to HIV, all the five dentists were promptly dealt with according to the in-hospital manual for needlestick injuries of Hiroshima University Hospital. Two dental residents opted to receive PEP (the dentist for case 1 received RAL + TDF/FTC [Raltegravir + Tenofovir /Emtricitabine] and the dentist for case 2 received RAL + TAF/FTC [Raltegravir + Tenofovir alafenamide /Emtricitabine]) and completed the full 4-week regimen without any side effects (Table 1). The three injures of the dentists were shallow, and they decided not to receive PEP after consultation with an HIV specialist. The HIV screening test was negative in all the HIV exposed dentists at the time of HIV exposure, and at 4 weeks and 12 weeks after the exposure (Table 1).

### 4. DISCUSSION

U=U indicates no risk of transmission of HIV by sexual activity without a condom in HIV-positive individuals who have maintained HIV viral load of less than 200 copies/mL for more than 6 months by continuing anti-HIV therapy.
[22-24]. It, however, remains unknown whether the U = U principle can also be applied to occupational exposures (such as needlestick injuries) in addition to sexual activity [41-43]. There are few reports on occupational exposures of HIV-positive patients and prognosis after the exposure at dental departments [44, 45]. To understand the relationship between U=U and occupational exposures, we have reported five cases of accidental occupational exposure to HIV. Occupational exposure of the dentists to the HIV-positive patients (case #1, 2, 4 and 5) whose HIV viral load was less than 20 copies/mL for more than 6 months, and to the HIV-positive patient whose HIV viral load was less than 20 copies/mL for 2 months (case #3) did not result in HIV transmission in any of the HIV-exposed dentists.

The PEP for HIV recommended by US PHS guidelines is expected to have a higher infection-blocking effect [33]. In fact, there are a few reports since 1999 of transmission from occupational exposures [46, 47]. The UK Chief Medical Officers’ Expert Advisory Group on AIDS does not recommend PEP for persons exposed to an HIV-infected person with a viral load of <200 copies HIV RNA/ml [48-50]. Although the dentists of cases 1 and 4 required PEP according to US PHS guidelines due to blood adhesion to the instrument responsible for the accident, the former took PEP and the latter did not. The dentist of case 2, on the other hand, did not need PEP according to the guidelines, although he still chose to take it. When focusing on exposure source patients according to UK guidelines, PEP for HIV is not required in all cases. However, our experience was before the revision of this guideline. Thus, it turned out that the decision to receive PEP robustly depends on the will of the dentist exposed to HIV.

CONCLUSION
In conclusion, to better understand the U=U concept of occupational exposures, we have reported five cases of accidental occupational exposure to HIV during dental treatment.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE
Approval of this study was obtained from the Institutional Review Boards (IRB) (Approval no. epidemiology -1485) at Hiroshima University, Japan.

HUMAN AND ANIMAL RIGHTS
No animals were used in this research. All humans research procedures were in accordance with the standards set forth in the Declaration of Helsinki principles of 1975, as revised in 2013 (http://ethics.iit.edu/ecodes/node/3931).

CONSENT FOR PUBLICATION
The studied participants were informed about the present research, and a written consent form was taken from all of them before their enrollment.

STANDARD OF REPORTING
The study conforms to the STROBE guidelines.

AVAILABILITY OF DATA AND MATERIALS
The authors confirm that the data supporting the results and findings of this study are available within the article.

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CONFLICT OF INTEREST
The authors declare no conflict of interest, financial or otherwise.

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