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LETTER ARTICLE

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.

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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

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Table 1. Clinical features of the study subjects.

Source Patients				Dental Professionals						
Case No.	CD4[a]	HIVRNA[b]	HIV Non-detection Period (mo.)[c]	Profession	Clinical Experience[d]	Instrument	Blood Adhesion	PEP	Side Effects	HIV Screening Test[h]
1	916	< 20	6	dentist	1	diamond bur	yes	RAL[e] + TDF/FTC[f]	none	negative
2	1898	< 20	12	dentist	1	explorer	no	RAL+ TAF/FTC[g]	none	negative
3	768	< 20	2	dentist	15	scissors	no	none	-	negative
4	1240	< 20	50	dentist	7	needle (30G)	yes	none	-	negative
5	1056	< 20	22	dentist	4	central incisor	no	none	-	negative

a. cells/ml
b. copy/ml
c. c. months
d. year(s)
e. RAL; Raltegravir
f. TDF/FTC; Tenofovir /Emtricitabine
g. TAF/FTC; Tenofovir alafenamide /Emtricitabine
h. Screening tests were performed at the time of HIV exposure, and 4 and 12 weeks after the exposure

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 #s 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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REFERENCES

[1] Morinaga K, Hagita K, Yakushiji T, Ohata H, Sueishi K, Inoue T. Analysis of needlestick and similar injuries over 10 years from April 2004 at Tokyo Dental College Chiba Hospital. Bull Tokyo Dent Coll 2016; 57(4): 299-305. http://dx.doi.org/10.2209/tdcpublication.2015-0036 PMID: 28049978

[2] Porter K, Scully C, Theyer Y, Porter S. Occupational injuries to dental personnel. J Dent 1990; 18(5): 258-62. http://dx.doi.org/10.1016/0300-5712(90)90025-A PMID: 2074298

[3] deVries B, Cossart YE. Needlestick injury in medical students. Med J Aust 1994; 160(7): 398-400. http://dx.doi.org/10.5694/j.1326-5377.1994.tb138262.x PMID: 8007860

[4] Chowanadisai S, Kukiattrakoon B, Yapong B, Kedjarune U, Leggat PA. Occupational health problems of dentists in southern Thailand. Int Dent J 2000; 50(1): 36-40. http://dx.doi.org/10.1111/j.1875-595X.2000.tb00544.x PMID: 10945178

[5] Schmid K, Schwager C, Drexler H. Needlestick injuries and other occupational exposures to body fluids amongst employees and medical students of a German university: incidence and follow-up. J Hosp Infect 2007; 65(2): 124-30. http://dx.doi.org/10.1016/j.jhin.2006.10.002 PMID: 17174445

[6] Stewardson DA, Palenik CJ, McHugh ES, Burke FJ. Occupational exposures occurring in students in a UK dental school. Eur J Dent Educ 2002; 6(3): 104-13. http://dx.doi.org/10.1034/j.1600-0579.2002.00253.x PMID: 12269865

[7] Wicker S, Rabenau HF. Occupational exposures to bloodborne viruses among German dental professionals and students in a clinical setting. Int Arch Occup Environ Health 2010; 83(1): 77-83. http://dx.doi.org/10.1007/s00420-009-0452-3 PMID: 19626335

[8] McDonald RI, Walsh LJ, Savage NW. Analysis of workplace injuries in a dental school environment. Aust Dent J 1997; 42(2): 109-13. http://dx.doi.org/10.1111/j.1834-7819.1997.tb00105.x PMID: 9153838

[9] Patterson JM, Novak CB, Mackinnon SE, Ellis RA. Needlestick injuries among medical students. Am J Infect Control 2003; 31(4): 226-30. http://dx.doi.org/10.1067/mic.2003.44 PMID: 12806360

[10] Leggat PA, Smith DR. Prevalence of percutaneous exposure incidents amongst dentists in Queensland. Aust Dent J 2006; 51(2):

158-61.
http://dx.doi.org/10.1111/j.1834-7819.2006.tb00420.x
PMID: 16848264

[11] Kobayashi K. Questionnaire study of needlestick injuries and hepatitis B vaccination in general dental practices. Jpn J Infec Prev Cont 2015; 30(5): 348-53.
http://dx.doi.org/10.4058/jsei.30.348

[12] Hirose A, Ozawa R, Ishizu E, *et al.* Investigation of needle sticks and incisions by medical workers in dental clinics. Jpn J Dent Prac Admin 2009; 43(4): 264-74.

[13] Yoneda M, Izumi T, Suzuki N, *et al.* Analysis of needlestick injuries in Fukuoka Dental College Medical and Dental Hospital. Jpn J Conserv Dent 2009; 52(2): 168-75.

[14] Bell DM. Occupational risk of human immunodeficiency virus infection in healthcare workers: an overview. Am J Med 1997; 102(5B): 9-15.
http://dx.doi.org/10.1016/S0002-9343(97)89441-7
PMID: 9845490

[15] Public Health Service guidelines for the management of healthcare worker exposures to HIV and recommendations for postexposure prophylaxis. MMWR Recomm Rep 1998; 47(RR-7): 1-33.
PMID: 9603630

[16] Updated U.S. Public Health Service guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for postexposure prophylaxis. MMWR Recomm Rep 2001; 50(RR-11): 1-52.
PMID: 11442229

[17] Ippolito G, Puro V, De Carli G. The risk of occupational human immunodeficiency virus infection in health care workers. Italian Multicenter Study. The Italian Study Group on Occupational Risk of HIV infection. Arch Intern Med 1993; 153(12): 1451-8.
http://dx.doi.org/10.1001/archinte.1993.00410120035005
PMID: 8512436

[18] Risk of sexual transmission of HIV from a person living with HIV who has an undetectable viral load https://www.preventionaccess.org/undetectable2016.

[19] Calabrese SK, Mayer KH. Providers should discuss U=U with all patients living with HIV. Lancet HIV 2019; 6(4): e211-3.
http://dx.doi.org/10.1016/S2352-3018(19)30030-X
PMID: 30772420

[20] Rendina HJ, Parsons JT. Factors associated with perceived accuracy of the Undetectable = Untransmittable slogan among men who have sex with men: Implications for messaging scale-up and implementation. J Int AIDS Soc 2018; 21(1)e25055
http://dx.doi.org/10.1002/jia2.25055 PMID: 29334178

[21] Vernazza P, Hirschel B, Bernasconi E, Flepp M. Les personnes séropositives ne souffrant d'aucune autre MST et suivant un traitment antirétroviral efficace ne transmettent pas le VIH par voie sexuelle
http://i-base.info/qa/wp-content/uploads/2008/02/Swiss-Commission-statement_May-2008_translation-EN.pdf2015.

[22] Rodger AJ, Cambiano V, Bruun T, *et al.* Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. Lancet 2019; 393(10189): 2428-38.
http://dx.doi.org/10.1016/S0140-6736(19)30418-0
PMID: 31056293

[23] Rodger AJ, Cambiano V, Bruun T, *et al.* Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. JAMA 2016; 316(2): 171-81.
http://dx.doi.org/10.1001/jama.2016.5148 PMID: 27404185

[24] Bavinton BR, Pinto AN, Phanuphak N, *et al.* Viral suppression and HIV transmission in serodiscordant male couples: an international, prospective, observational, cohort study. Lancet HIV 2018; 5(8): e438-47.
http://dx.doi.org/10.1016/S2352-3018(18)30132-2
PMID: 30025681

[25] Cohen MS, Chen YQ, McCauley M, *et al.* Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011; 365(6): 493-505.
http://dx.doi.org/10.1056/NEJMoa1105243 PMID: 21767103

[26] Quinn TC, Wawer MJ, Sewankambo N, *et al.* Viral load and heterosexual transmission of human immunodeficiency virus type 1. N Engl J Med 2000; 342(13): 921-9.
http://dx.doi.org/10.1056/NEJM200003303421303
PMID: 10738050

[27] Attia S, Egger M, Müller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. AIDS 2009; 23(11): 1397-404.
http://dx.doi.org/10.1097/QAD.0b013e32832b7dca
PMID: 19381076

[28] Beekmann SE, Henderson DK. Prevention of HIV/AIDS: Post-Exposure Prophylaxis (including Healthcare Workers). Infect Dis Clin North Am 2014; 28(4): 601-13.
http://dx.doi.org/10.1016/j.idc.2014.08.005 PMID: 25287589

[29] Elliott T, Sanders EJ, Doherty M, *et al.* Challenges of HIV diagnosis and management in the context of pre-exposure prophylaxis (PrEP), post-exposure prophylaxis (PEP), test and start and acute HIV infection: a scoping review. J Int AIDS Soc 2019; 22(12)e25419
http://dx.doi.org/10.1002/jia2.25419 PMID: 31850686

[30] Thomas R, Galanakis C, Vézina S, *et al.* Adherence to Post-Exposure Prophylaxis (PEP) and incidence of HIV seroconversion in a major North American Cohort. PLoS One 2015; 10(11)e0142534
http://dx.doi.org/10.1371/journal.pone.0142534 PMID: 26559816

[31] Ford N, Irvine C, Shubber Z, *et al.* Adherence to HIV postexposure prophylaxis: a systematic review and meta-analysis. AIDS 2014; 28(18): 2721-7.
http://dx.doi.org/10.1097/QAD.0000000000000505
PMID: 25493598

[32] Cardo DM, Culver DH, Ciesielski CA, *et al.* A case-control study of HIV seroconversion in health care workers after percutaneous exposure. N Engl J Med 1997; 337(21): 1485-90.
http://dx.doi.org/10.1056/NEJM199711203372101
PMID: 9366579

[33] Shih CC, Kaneshima H, Rabin L, *et al.* Postexposure prophylaxis with zidovudine suppresses human immunodeficiency virus type 1 infection in SCID-hu mice in a time-dependent manner. J Infect Dis 1991; 163(3): 625-7.
http://dx.doi.org/10.1093/infdis/163.3.625 PMID: 1995734

[34] Tsai CC, Emau P, Follis KE, *et al.* Effectiveness of postinoculation (R)-9-(2-phosphonylmethoxypropyl) adenine treatment for prevention of persistent simian immunodeficiency virus SIVmne infection depends critically on timing of initiation and duration of treatment. J Virol 1998; 72(5): 4265-73.
http://dx.doi.org/10.1128/JVI.72.5.4265-4273.1998
PMID: 9557716

[35] Kuhar DT, Henderson DK, Struble KA, *et al.* Updated US Public Health Service guidelines for the management of occupational exposures to human immunodeficiency virus and recommendations for postexposure prophylaxis. Infect Control Hosp Epidemiol 2013; 34(9): 875-92.
http://dx.doi.org/10.1086/672271 PMID: 23917901

[36] Deguchi M, Yoshioka N, Kagita M, *et al.* Evaluation of human immunodeficiency virus-1/2 antigen/antibody immunochromatographic assay. Clin Lab 2012; 58(11-12): 1193-201.
PMID: 23289189

[37] Sekiguchi H, Ayabe A, Ohta A, Ishibashi M. Evaluation of the 4th generation HIV rapid diagnostic kit 'ESPLINE HIV Ag/Ab'. Jpn J Med Pharm Sci 2010; 63(4): 673-80.

[38] Kawahata T, Nagashima M, Sadamasu K, Kojima Y, Mori H. [Evaluation of an immunochromatographic fourth generation test for the rapid diagnosis of acute HIV infection]. Kansenshogaku Zasshi 2013; 87(4): 431-4.
http://dx.doi.org/10.11150/kansenshogakuzasshi.87.431
PMID: 23984592

[39] Faraoni S, Rocchetti A, Gotta F, *et al.* Evaluation of a rapid antigen and antibody combination test in acute HIV infection. J Clin Virol 2013; 57(1): 84-7.
http://dx.doi.org/10.1016/j.jcv.2013.01.007 PMID: 23380659

[40] Brauer M, De Villiers JC, Mayaphi SH. Evaluation of the Determine™ fourth generation HIV rapid assay. J Virol Methods 2013; 189(1): 180-3.
http://dx.doi.org/10.1016/j.jviromet.2013.01.017

PMID: 23391823

[41] Waitt C, Low N, Van de Perre P, Lyons F, Loutfy M, Aebi-Popp K. Does U=U for breastfeeding mothers and infants? Breastfeeding by mothers on effective treatment for HIV infection in high-income settings. Lancet HIV 2018; 5(9): e531-6. http://dx.doi.org/10.1016/S2352-3018(18)30098-5 PMID: 29960731

[42] U=U taking off in 2017. Lancet HIV 2017; 4(11)e475 http://dx.doi.org/10.1016/S2352-3018(17)30183-2 PMID: 29096785

[43] Leylabadlo HE, Baghi HB, Fallahi L, Kafil HS. From sharing needles to unprotected sex: a new wave of HIV infections in Iran? Lancet HIV 2016; 3(10): e461-2. http://dx.doi.org/10.1016/S2352-3018(16)30158-8 PMID: 27687040

[44] Klein RS, Phelan JA, Freeman K, *et al.* Low occupational risk of human immunodeficiency virus infection among dental professionals. N Engl J Med 1988; 318(2): 86-90. http://dx.doi.org/10.1056/NEJM198801143180205 PMID: 3422106

[45] Ippolito G, Puro V, Heptonstall J, Jagger J, De Carli G, Petrosillo N. Occupational human immunodeficiency virus infection in health care workers: worldwide cases through September 1997. Clin Infect Dis 1999; 28(2): 365-83. http://dx.doi.org/10.1086/515101 PMID: 10064256

[46] Joyce MP, Kuhar D, Brooks JT. Notes from the field: occupationally acquired HIV infection among health care workers - United States, 1985-2013. MMWR Morb Mortal Wkly Rep 2015; 63(53): 1245-6. [MMWR]. PMID: 25577991

[47] Tomkins S, Ncube F. Occupationally acquired HIV: international reports to December 2002. Eurosurveillance Weekly 2005; 10(10)

[48] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/275060/EAGA_advice_on_PEP_after_exposure_to_UD_source_Dec13.pdf2013.

[49] Puro V, Cicalini S, De Carli G, *et al.* Post-exposure prophylaxis of HIV infection in healthcare workers: recommendations for the European setting. Eur J Epidemiol 2004; 19(6): 577-84. http://dx.doi.org/10.1023/B:EJEP.0000032349.57057.8a PMID: 15330131

[50] HIV Post-exposure prophylaxis: Guidance from the UK Chief Medical Officers' Expert Advisory Group on AIDS. Department of Health 2008.