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Research paper

Drug use and the risk of HIV infection amongst injection drug users participating in an HIV vaccine trial in Bangkok, 1999–2003☆,☆☆

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ABSTRACT

Background: HIV spread rapidly amongst injecting drug users (IDUs) in Bangkok in the late 1980s. In recent years, changes in the drugs injected by IDUs have been observed. We examined data from an HIV vaccine trial conducted amongst IDUs in Bangkok during 1999–2003 to describe drug injection practices, drugs injected, and determine if drug use choices altered the risk of incident HIV infection.
Methods: The AIDSVAX B/E HIV vaccine trial was a randomized, double-blind, placebo-controlled trial. At enrolment and every 6 months thereafter, HIV status and risk behaviour were assessed. A proportional hazards model was used to evaluate demographic characteristics, incarceration, drug injection practices, sexual activity, and drugs injected during follow-up as independent predictors of HIV infection.
Results: The proportion of participants injecting drugs, sharing needles, and injecting daily declined from baseline to month 36. Amongst participants who injected, the proportion injecting heroin declined (98.6–91.9%), whilst the proportions injecting methamphetamine (16.2–19.6%) and midazolam (9.9–31.9%) increased. HIV incidence was highest amongst participants injecting methamphetamine, 7.1 (95% CI, 5.4–9.2) per 100 person years. Injecting heroin and injecting methamphetamine were independently associated with incident HIV infection.
Conclusions: Amongst AIDSVAX B/E vaccine trial participants who injected drugs during follow-up, the proportion injecting heroin declined whilst the proportion injecting methamphetamine, midazolam, or combinations of these drugs increased. Controlling for heroin use and other risk factors, participants injecting methamphetamine were more likely to become HIV-infected than participants not injecting methamphetamine. Additional HIV prevention tools are urgently needed including tools that address methamphetamine use.

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☆ Clinical trial registration: The AIDSVAX B/E HIV vaccine trial is registered at ClinicalTrials.gov http://clinicaltrials.gov/ct2/show/NCT00006327?term=AIDSVAX&rank=6 ClinicalTrials.gov Identifier: NCT00006327.

☆☆ Disclaimer: The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the U.S. Centers for Disease Control and Prevention.

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Background

HIV spread rapidly amongst injecting drug users (IDUs) in Bangkok in the late 1980s and HIV prevalence has remained high, 30–50%, through 2004 (Thailand Ministry of Public Health, 2006; Weniger, Limpakarnjanarat, & Ungchusak, 1991). Heroin was the predominant drug injected by IDUs during the 1980s and 1990s (Vanichseni, Kitayaporn, & Mastro, 2001; Weniger et al., 1991) but in recent years, declines in heroin use and increases in methamphetamine and midazolam use have been observed (van Griensven, Pitisuttithum, & Vanichseni, 2005).

Methamphetamine is a highly addictive stimulant and its use has been linked to increases in HIV-associated risk behaviour and incident HIV infections amongst men who have sex with men (Buchacz, McFarland, & Kellogg, 2005; Colfax, Mansergh, & Guzman, 2001; Drumright, Little, & Strathdee, 2006; Koblin, Husnik, & Colfax, 2006; Plankey, Ostrow, & Stall, 2007; Shoptaw & Reback, 2006; Shoptaw & Reback, 2007; Taylor, Aynalem, Smith, Montoya, & Kerndt, 2007; Waldo, McFarland, Katz, MacKellar, & Valleroy, 2000; Woody, Donnell, & Seage, 1999), men who have sex with women (CDC, 2006; Wohl, Johnson, & Lu, 2002), and female sex workers (Patterson, Semple, & Staines, 2008). A study amongst IDUs in North America found a significant increase of methamphetamine injection during 1996–2004 and an independent association of methamphetamine injection with HIV-associated risk behaviour (Fairbairn et al., 2007).

Midazolam use has also been associated with increases in risk behaviour amongst IDUs (van Griensven et al., 2005). Midazolam, marketed as Versed and Dormicum, is a short-acting benzodiazepine with potent sedative and amnestic effects (Roche Laboratories, 1999). It is used to induce drowsiness and relieve anxiety prior to surgery and to decrease memory of perioperative events. In Thailand, a physician's prescription is required to obtain midazolam.

The Bangkok Metropolitan Administration (BMA), the city government of Bangkok, operates 17 drug-treatment clinics that offer a range of services to IDUs including HIV voluntary counselling and testing, risk-reduction counselling, social and welfare services, health education, primary medical care and referrals, methadone treatment, condoms, and bleach to clean injection equipment with demonstrations and instructions on appropriate use. Clinics provide these services free of charge. Thailand's narcotics law prohibits the distribution of needles and syringes to IDUs and needles are not provided in the drug-treatment clinics; however, sterile needles and syringes are available to the public over the counter at low cost (5–10 baht/0.12–0.25 USD) in pharmacies in Bangkok.

An HIV vaccine trial was conducted amongst IDUs at the BMA drug-treatment clinics during 1999–2003 (Pitisuttithum, Gilbert, & Gurwith, 2006). The vaccine, AIDSVAX B/E, did not prevent HIV infection but important trial findings included significant declines in participant reports of injection drug use, needle sharing, and daily injection during follow-up (van Griensven, Keawkungwal, & Tappero, 2004) and an association between incarceration in jail and incident HIV infection (Suntharasamai, Martin, & Vanichseni, 2009). Based on evidence linking methamphetamine and midazolam use to HIV-associated risk behaviour and changes in drugs injected by IDUs in Bangkok, we reviewed data from the AIDSVAX B/E trial to more fully describe drugs injected by trial participants and to determine if drug use choices altered the risk of incident HIV infection.

Methods

The AIDSVAX B/E HIV vaccine trial was a randomized, double-blind, placebo-controlled trial conducted amongst IDUs at 17 Bangkok Metropolitan Administration drug-treatment clinics (Pitisuttithum et al., 2006; Vanichseni, Tappero, & Pitisuttithum, 2004). Briefly, 2546 HIV-uninfected IDUs 20–60 years old enrolled and were randomized (1:1) to receive AIDSVAX B/E or placebo. A total of 2295 (90.1%) participants were followed through month 36 or until HIV infection. At enrolment and every 6 months thereafter, staff collected blood for HIV testing, provided risk-reduction counselling, and administered a standardized questionnaire to assess drug injection practices, drugs injected, sexual activity, and incarceration during the previous 6 months. Staff did not ask participants about non-injection drug use. Participant blood specimens were tested for HIV infection using Genetic Systems-Biorak ELISA and Western blot. HIV RNA nucleic acid-based amplification testing was done on the participant blood specimen collected at the visit immediately preceding the positive ELISA and Western blot result to limit time from exposure to laboratory confirmed HIV infection and more accurately define the first HIV positive visit.

We used SAS (Version 9; SAS Institute, Cary, NC, USA) for the following analyses. Generalized estimation equation logistic regression was used to evaluate drug injection practices and drugs injected during follow-up (Diggle, Liang, & Zeger, 1994). HIV incidence was calculated per 100 person years of HIV-negative observation based on HIV status at 6-month visits and exact 95% Poisson confidence intervals (CI) were calculated. A discrete time proportional hazards model was used to evaluate demographic characteristics at baseline and incarceration, drug injection practices, sexual activities, and drugs injected during the 6 months preceding follow-up study visits as predictors of HIV infection (Cox, 1972). We assumed that HIV infection was associated with behaviours or events that occurred during 6 months before the visit when HIV infection was diagnosed.

Amongst participants who reported injecting drugs at 6-month follow-up visits, >99% reported injecting heroin, methamphetamine, or midazolam, or combinations of these drugs. Therefore, we used these drugs in the proportional hazards model. Variables that were associated with HIV infection in bivariate analysis ($p < 0.1$) and drugs injected (i.e., heroin, methamphetamine, midazolam) were evaluated in a multivariable model. We created interaction terms to evaluate associations between each combination of drugs injected (i.e., heroin and methamphetamine, heroin and midazolam, methamphetamine and midazolam) and HIV infection and between sharing needles, the drug injected (i.e., heroin, methamphetamine, and midazolam) and HIV infection. Reports of injecting any drugs and injecting heroin were co-linear (i.e., amongst all reports of injecting, 96.8% included heroin) and could not be evaluated independently.

The trial was conducted with the understanding and consent of each participant. The trial protocol and consent forms were approved by Ethical Review Committees of the Thailand Ministry of Public Health, Bangkok Metropolitan Administration, and Mahidol University and an Institutional Review Board of the U.S. Centers for Disease Control and Prevention.

Results

Participants were predominantly male (93.4%) with a median age of 26 years (range, 20–59 years). Most (67.3%) had completed 9 years of school or more. At baseline, 93.8% of participants reported they had injected drugs during the past 6 months; 31.0% had shared needles and 36.8% injected drugs daily (Table 1). Incarceration was common with 53.9% of participants reporting incarceration during the trial. During follow-up, 211 (8.3%) participants became HIV-infected yielding an HIV incidence rate of 3.4 (95% CI, 3.0–3.9) per 100 person years. There was no evidence of a calendar-time trend in incidence. One participant tested HIV-seropositive