Educating Correctional Health Care Providers and Inmates About Drug-Drug Interactions: HIV-Medications and Illicit Drugs

Abe Macher[1], Deborah Kibble[2], Karen Bryant[3], Ana Cody[4], Todd Pilcher[5], Danielle Jahn[6]

[1]*U.S. Department of Health and Human Services*
[2]*Prince William Manassas Regional Adult Detention Center*
[3]*Hospice of the Chesapeake*
[4]*La Clinica del Pueblo*
[5]*Whitman Walker Clinic*
[6]*Office of the Federal Public Defender for the District of Columbia*

Abstract

This paper demonstrates how federal clinicians are collaborating with correctional health care providers in a unique continuing education initiative regarding HIV-medications and drug-drug interactions. Three clinical cases are presented to illustrate the potential dangers associated with concomitant use of ritonavir (a frequently prescribed antiretroviral agent) and illicit drugs. Such clinical cases are regularly presented in an exemplar program that draws clinicians together to share current medical information and notes "from the field" regarding problems that correctional health care providers and administrators are likely to face. Collaboration between federal clinicians, correctional and community health officials has resulted in a unique forum for disseminating medical information, and represents a prototypical method for broad-based health education.

Keywords: drug interactions, correctional health care providers, illicit drugs, antiretroviral agents

The Challenges of Correctional Health Care

The National Commission on Correctional Health Care (NCCHC) has provided estimates for the numbers of inmates released with communicable diseases and the percentages relative to the United States population with those infections. Data from 1996 revealed that at least 1.3 million inmates released from correctional facilities in that year were infected with hepatitis C virus (HCV) (NCCHC, 2002) and these former inmates represented 29 percent of all U.S. cases of HCV infection. Hepatitis B virus (HBV) infection, on the other hand, was found in 155,000 released inmates, accounting for 15.5 percent of all U.S. cases. Significant fractions of HIV infection (98,000; 13 percent) and AIDS cases (39,000; 17 percent) were also reported among persons released from jails and prisons. It has been estimated that approximately one fourth of all HIV-infected persons in the U.S. pass through the corrections system each year (Laurence, 2005; NCCHC, 2002).

Since the clinical management of HIV disease and hepatitis is constantly evolving, correctional health care providers and health services administrators must have access to continuing medical education. This paper examines a pilot continuing-education-project in Washington, D.C., that involves collaboration between federal clinicians, correctional providers, and health services administrators. The Correctional Health Care Subcommittee is composed of representatives from correctional facilities in Virginia, Maryland, and the District of Columbia. Dr. Abe Macher, who serves as a volunteer clinical consultant to the Sub-committee, has recruited representatives from the Federal Bureau of Prisons, the U.S. Marshals Service, the Veterans Administration, the Office of the Federal Public Defender for the District of

Columbia, the Centers for Disease Control and Prevention, local and state departments of health, community-based clinics, and hospice organizations (see Table 1) to participate in monthly multidisciplinary meetings where clinical cases are presented and discussed. State-of-the-art treatment updates regarding HIV/AIDS, hepatitis, bioterrorism, methicillin-resistant Staphylococcus aureus, tuberculosis and other infectious disease issues are presented at each meeting.

Table 1
Participants of the Metropolitan Washington Council of Governments' Correctional Health Care Subcommittee Meetings

City, County, and Regional Detention Centers
State Departments of Corrections
Federal Bureau of Prisons
U.S. Marshals Service
Office of the Federal Public Defender for the District of Columbia
Health Resources and Services Administration, U.S. Public Health Service
Centers for Disease Control and Prevention, U.S. Public Health Service
Veterans Administration
County and State Departments of Health
Community-Based HIV Clinics (e.g., La Clinica del Pueblo; Whitman Walker)
AIDS Drug Assistance Programs
Hospice of the Chesapeake
University and Community Hospitals
American Correctional Association
American Jail Association
Public Safety Division, Council of Governments

A major concern of the Subcommittee is the proper use of FDA-approved HIV-medications and their potential toxicities and drug-drug interactions. An emerging dilemma within the metropolitan Washington, D.C. area is the interaction between prescribed HIV-medications (e.g., ritonavir) and illicit drugs such as hallucinogenic amphetamine derivatives (e.g., Methamphetamine; Ecstasy). Since a considerable number of HIV-infected inmates and former inmates are polysubstance abusers, they are at considerable risk for drug-drug interactions between their prescribed HIV-medications and illicit drugs. In addition to educating the correctional providers and administrators, physicians educate inmates, focusing on post-release continuity of antiretroviral treatment and avoidance of illicit (interactive) drugs.

Inter-Agency Collaborative Education: An Exemplar Program

In 1998, the Congressional Black Caucus declared HIV/AIDS a medical emergency among indigent African-Americans, and highlighted the problem within our nation's correctional facilities. The Caucus requested volunteers from the United States Public Health Service (USPHS) to provide clinical assistance. Dr. Macher, a USPHS physician, volunteered to create a regional correctional HIV program, and volunteered to serve as clinical consultant to the

Metropolitan Washington Council of Governments' Correctional Health Care Subcommittee. He recruited clinicians from the region to join the Subcommittee. Since 1998, the Subcommittee has been meeting on a monthly basis to address HIV/AIDS as well as other infectious disease issues, including bioterrorism. Dr. Macher presents patients' clinical cases at each meeting of the Subcommittee. The following three clinical cases focus on drug-drug interactions between the prescribed antiretroviral agent ritonavir and illicit drugs.

Clinical Case One: Ecstasy and Ritonavir

The patient, a man with HIV-infection with a history of alcohol abuse and illicit use of "Ecstasy"(3,4 methylenedioxymethamphetamine or street names of MDMA; XTC; X; M; E; Clarity; Adam; Essence; Ecky; Bicky; Yaoto-Wang) was prescribed an antiretroviral treatment regimen that included the protease inhibitor ritonavir. Two weeks after starting treatment with ritonavir, he went to a club and took three MDMA (Ecstasy) tablets. In the past (prior to being prescribed ritonavir) he had taken MDMA on several occasions without untoward effects.

Four hours after his arrival at the club, a nurse noted that he was hypertonic, sweating profusely, tachypneic (approximately 45 breaths per minute), tachycardic (in excess of 140 beats per minute), and cyanosed. He was able to talk in full sentences and gave a history of having taken two MDMA tablets with little effect, so he took a further half-tablet (estimated total dose 180 mg MDMA, calculated from the MDMA content of the remaining half tablet), after which he began to "feel shaky." Within 25 minutes of the first assessment he had an apparent tonic-clonic convulsion, but was able to respond to questions. He became increasingly tachypneic, and his carotid pulse rate was approximately 200 per minute. A few minutes later he vomited and had a cardiopulmonary arrest. Attempts at resuscitation were unsuccessful.

Postmortem toxicology revealed MDMA in his blood at a concentration of 4.56 mg/L (ten times the anticipated concentration). The protease inhibitor ritonavir is an inhibitor of cytochrome P450 2D6 (CYP2D6), an isoenzyme responsible for demethylenation – the principal pathway by which MDMA is metabolized. Thus, ingestion of MDMA in recreational amounts by a person taking ritonavir can lead to toxic effects due to high plasma concentrations of MDMA. This patient's death was consistent with a severe serotoninergic reaction to MDMA. Adverse effects of MDMA ingestion result from sympathetic overload and include tachycardia, diaphoresis, tremor, hypertension, arrhythmias, parkinsonism, and urinary retention. The most serious potential outcome of MDMA ingestion is hyperthermia and the associated "serotonin syndrome" manifested by grossly elevated core body temperature, rigidity, myoclonus, and autonomic instability; patients may develop rhabdomyolysis and acute renal failure, hepatic failure, adult respiratory distress syndrome, and coagulopathy (Gahlinger 2004).

Clinical Case Two: Methamphetamine, Amyl Nitrate, and Ritonavir

A man with HIV-infection and a history of recreational drug use was prescribed an antiretroviral treatment regimen that included ritonavir. Four months later, he was witnessed injecting himself twice with methamphetamine (Meth, Crystal) as well as sniffing amyl nitrate. His friends left him at approximately 3:00 a.m., apparently asleep, lying on his stomach on the floor. The next day he was found dead in the same position in which he had been left.

Postmortem toxicology detected meth-amphetamine at a level of 0.5 mg/L in his blood (Hales, Roth, & Smith, 2000). This patient had also been abusing amyl nitrate. Amyl nitrate is metabolized to nitric oxide which inhibits cytochrome P450, and ritonavir inhibits CYP2D6 which has a major role in methamphetamine metabolism. These drug-drug interactions probably led to the high plasma concentrations of methamphetamine.

Clinical Case Three: Ecstasy, GHB, and Ritonavir

A man with HIV-infection began taking an antiretroviral treatment regimen that included ritonavir. Harrington, Woodward, Hooton, and

Horn (1999, p. 2221) reported that five days later the following occurred:

> Twenty minutes after ingesting a half teaspoon of "Liquid Ecstasy" (gamma-hydroxybutyrate, or GHB), the man became unresponsive and exhibited a brief episode of repetitive, clonic contractions of both legs and then the left side of his body. Emergency medical personnel found him responsive only to painful stimuli, with shallow respirations and a heart rate of only 40 per minute. He was endotracheally intubated and transferred to a local hospital. A toxicology screen was positive for methamphetamine and MDMA. During the next three hours, his vital signs normalized and he woke up and extubated himself. Upon questioning, he admitted to ingesting two MDMA tablets approximately 29 hours prior to admission. Six hours prior to admission, he ingested one half teaspoon of GHB, and a similar dose of GHB immediately before becoming unconscious. He stated that he took the GHB to counter the agitating effects of MDMA, which had persisted for more than one day after ingestion. The patient noted that prior to his use of ritonavir, he had taken a similar quantity of GHB as a sleep aide on many occasions and he had never experienced any adverse reactions. He also noted that his friends had consumed similar amounts of the same preparation of GHB every two to three hours without any adverse effects.
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> The patient maintained that the duration (>29 hours) of the stimulatory effect of the MDMA he ingested was much longer than when he had taken similar doses of MDMA in the past (prior to his antiretroviral treatment with ritonavir). He explained that the sustained effects of MDMA are what prompted him to take GHB, given its sedating qualities. He proceeded to experience clinical features typical of GHB poisoning with a rapid onset of loss of consciousness, seizure-like activity, and respiratory depression. Ritonavir probably inhibited the metabolism of both MDMA and GHB in this patient.

Discussion

These three clinical cases underscore the hazards of mixing illicit drugs with prescribed HIV-medications. Given the variations in drug absorption and metabolism that exist between individuals, it is impossible to accurately predict the effect of drug combinations in any one person. This is particularly important with regard to the use of illicit drugs, which are often taken by groups of people. Individuals within the group may be falsely reassured by others that such drug combinations are safe.

A prudent approach for HIV providers would be to caution their patients that the known and potential drug interactions between illicit substances and HIV-medications are complex and unpredictable. Co-administration of HIV-medications with illicit substances should be strongly discouraged. Consequently, correctional health care providers should utilize each clinical visit with their inmate-patients as opportunities for ongoing continuing education and preparation for post-release continuity-of-care.

Conclusions

Each year, some 630,000 persons are released from state and federal prisons (Office of Justice Programs, 2005). Moreover, another 13.6 million persons are arrested, and are admitted and discharged from county jails and juvenile detention centers (Federal Bureau of Investigation, 2004). Rates of illicit drug use in this population are very high (see James, 2004), and these detainees and inmates also engage in other risky behaviors.

Following admission to a correctional facility, inmates represent a "captive audience" and interventions that attempt to reduce their risky behaviors should be undertaken. Correctional officials and clinicians must first, however, have a clear understanding of the risks that their populations are likely to engage. The correctional health care initiative in Washington, DC, is an exemplar program that unites local, state, and federal agencies and organizations and promotes ongoing education, communication, cooperation, collaboration, and continuity-of-care. We recommend that correctional facilities unite in their respective regions by accessing

their local Councils of Governments (or equivalent organizations) and pooling their area's clinical and educational resources (Macher et al., 2002).

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Author Information
Abe Macher
U.S. Department of Health and Human Services
E-Mail: AMacher@hrsa.gov

Deborah Kibble
Prince William Manassas Regional Adult Detention Center

Karen Bryant
Hospice of the Chesapeake

Ana Cody
La Clinica del Pueblo

Todd Pilcher
Whitman Walker Clinic

Danielle Jahn
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