

Interactions between HIV-Related Medications and Methadone:

An Overview

MARC N. GOUREVITCH, M.D., M.P.H.

Updated March 2001

Adapted and updated by MN Gourevitch from an article originally published as: Gourevitch MN, Friedland GF. Interactions between methadone and medications used to treat HIV infection: A review. Mt Sinai J Med 2000; 67:429–436.

TABLE

Medication	Formally Studied?	Effect on Methadone	Effect on HIV-Related Medication	Reference
NRTI				
Zidovudine (AZT)	Yes	None	↑ AZT AUC by 40%	(1, 2)
Didanosine (ddI)	Yes	None	↓ ddI AUC by 60%	(3)
Zalcitabine (ddC)	No	Not studied or reported	Not studied or reported	
Stavudine (d4T)	Yes	None	↓ d4T AUC by 18%	(3)
Lamivudine (3TC)	Yes	None	Not studied	(4)
Abacavir (ABC)	Yes	↑ Methadone clearance	↑ Time to peak concentration ↓ Peak concentration	(5)
NNRTI				
Nevirapine	Yes	Withdrawal symptoms ↓ Methadone levels by 46%	Not studied or reported	(6–8)
Delavirdine	No	Need for ↑ methadone dose observed ↑ Methadone levels predicted	Not studied or reported	
Efavirenz	Yes	↓ Methadone levels by 48%	Not studied or reported	(8, 9)
PI				
Indinavir	No	Not reported	Not reported	
Ritonavir	Yes	↓ Methadone levels reported† ↓ Meperidine levels	No effect reported †	(10) (11)
Nelfinavir	Yes	↓ Methadone levels, but no withdrawal symptoms observed	No	(12)
Saquinavir	Planned	Not studied or reported	Not studied or reported	
Amprenavir*	Yes	↓ Methadone levels, but no withdrawal symptoms observed	Not studied or reported	(13)
Lopinavir*	PDR data only	↓ Methadone levels reported†	Not studied or reported	(14)
Other medications used in the treatment of HIV-infected persons				
Rifampin	Yes	↓ Methadone levels, often sharply	None reported	(15)
Rifabutin	Yes	No change in methadone levels	None reported	(16)
Fluconazole	Yes	Mild narcotic withdrawal symptoms ↑ Methadone levels by approximately 30%, clinical significance unknown	None reported	(17)
Phenytoin	Yes	↓ Methadone levels, often sharply	None reported	(18)
Phenobarbital	Yes	↓ Methadone levels, often sharply	None reported	(19)
Carbamazepine	Yes	↓ Methadone levels	None reported	(20)
Fluvoxamine*	No (case series only)	↓ Methadone levels by 20–100%	None reported	(21, 22)
Fluoxetine*	No (case series only)	Minimal ↑ methadone levels	None reported	
Sertraline*	Yes	Transient mild ↑ methadone levels	None reported	(23)

NRTI = nucleoside reverse transcriptase inhibitors

NNRTI = non-nucleoside reverse transcriptase inhibitors

PI = protease inhibitor

AUC = area under curve

† Study design limits clinical utility of results.

* New

References

1. Schwartz EL, Brechbühl AB, Kahl P, et al. Pharmacokinetic interactions of zidovudine and methadone in intravenous drug-using patients with HIV infections. *J Acquir Immune Defic Syndr* 1992; 5:619–626.
2. McCance-Katz EF, Rainey PM, Jatlow P, Friedland GH. Methadone effects on zidovudine disposition (AIDS Clinical Trials Group 262). *J Acquir Immune Defic Syndr* 1998; 18:435–443.
3. Rainey PM, Friedland GH, McCance EF, et al. Interaction of methadone with didanosine (ddI) and stavudine (d4T). *J AIDS Hum Retrovirology* 2000; 24:241–248.
4. Rainey PM, Friedland G, Snidow J, et al. Effects of zidovudine plus lamivudine on methadone disposition. 101st Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics; 2000 Mar 15–17; Los Angeles, CA. Abstract PIII-94.
5. Sellers E, Lam R, McDowell J, et al. The pharmacokinetics (PK) of abacavir (ABC) and methadone (M) following co-administration: CNA1012. 39th Interscience Conference on Antimicrobial Agents and Chemotherapy; 1999 Sep 26–29; San Francisco, CA. Abstract No. 305.
6. Staszewski S, Haberl A, Gute P, et al. Nevirapine/didanosine/lamivudine once daily in HIV-1-infected intravenous drug users. *Antiviral therapy* 1998; 3(Suppl 4):55–56.
7. Altice FL, Friedland GH, Cooney EL. Nevirapine induced opiate withdrawal among injection drug users with HIV infection receiving methadone. *AIDS* 1999; 13:957–962.
8. Clarke S, Mulcahy F, Back D, et al. Managing methadone and non-nucleoside reverse transcriptase inhibitors: guidelines for clinical practice. Seventh Conference on Retroviruses and Opportunistic Infections; 2000 Jan 30–Feb 2; San Francisco, CA. Abstract No. 88.
9. Tashima K, Bose T, Gormley J, et al. The potential impact of efavirenz on methadone maintenance. Ninth European Congress of Clinical Microbiology and Infectious Diseases; 1999 Mar 21–24; Berlin, Germany. Abstract No. P0552.
10. Hsu A, Granneman GR, Carothers L, et al. Ritonavir does not increase methadone exposure in healthy volunteers. Fifth Conference on Retroviruses and Opportunistic Infections; 1998 Feb 1–5; Chicago IL. Abstract No. 324.
11. Piscitelli S, Rock-Kress D, Bertz R, et al. Ritonavir decreases meperidine exposure in HIV-negative subjects. Sixth Conference on Retroviruses and Opportunistic Infections; 1999 Jan 31–Feb 4; Chicago, IL. Abstract No. 373.
12. Hsyu PH, Lillibridge JH, Maroldo L, et al. Pharmacokinetic (PK) and pharmacodynamic (PD) interactions between nelfinavir and methadone. Seventh Conference on Retroviruses and Opportunistic Infections; 2000 Jan 30–Feb 2; San Francisco, CA. Abstract No. 87.
13. Hendrix C, Wakeford J, Wire MB, et al. Pharmacokinetic and pharmacodynamic evaluation of methadone enantiomers following co-administration with amprenavir in opioid-dependent subjects. 40th Interscience Conference on Antimicrobial Agents and Chemotherapy; 2000 Sep 17–20; Toronto, Ontario, Canada. Abstract 1649.
14. Kaletra Product Information. Abbott Laboratories, Inc., North Chicago, IL, 2000.
15. Kreek MJ, Garfield JW, Gutjahr CL, Giusti LM. Rifampin-induced methadone withdrawal. *N Engl J Med* 1976; 294:1104–1106.
16. Brown LS, Sawyer RC, Li R, et al. Lack of pharmacologic interaction between rifabutin and methadone in HIV-infected former injecting drug users. *Drug Alcohol Depend* 1996; 43:71–77.
17. Cobb M, Desai J, Brown LS, et al. The effect of fluconazole on the clinical pharmacokinetics of methadone. *Clinical Pharmacol Ther* 1998; 63:655–662.
18. Tong TG, Pond SM, Kreek MJ, et al. Phenytoin-induced methadone withdrawal. *Ann Intern Med* 1981; 94:349–351.
19. Liu SJ, Wang RI. Case report of barbiturate-induced enhancement of methadone metabolism and withdrawal syndrome. *Am J Psychiatry* 1984; 141:1287–1288.
20. Saxon AJ, Whittaker S, Hawker SC. Valproic acid, unlike other anticonvulsants, has no effect on methadone maintenance: Two cases. *J Clin Psychiatry* 1989; 50:228–229.
21. Bertschy G, Baumann P, Eap CB, Baettig D. Probable metabolic interaction between methadone and fluvoxamine in addict patients. *Ther Drug Monit* 1994; 16:42–45.
22. DeMaria PA, Serota RD. A therapeutic use of the methadone fluvoxamine drug interaction. *J Addict Dis* 1999; 18:5–12.
23. Hamilton SP, Nunes EV, Janal M, Weber L. The effect of sertraline on methadone plasma levels in methadone-maintained patients. *Am J Addict* 2000; 9:63–69.