CLINICAL REVIEW

BRIEF REPORT: Methadone Treatment of Injecting Opioid Users for Prevention of HIV Infection

Linda R. Gowing, PhD,[1] Michael Farrell, MRCP, MRCPsych[2] Reinhard Bornemann, MD, DrPH, PhD[3] Lynn E. Sullivan, MD[4] Robert L. Ali, MBBS, FAFPHM, FAChAM, GDPH[1]

[1]University of Adelaide and Drug and Alcohol Services, South Australia, Australia; [2]National Addiction Centre, UK; [3]Universitaet Bielefeld, Bielefeld, Germany; [4]Yale University School of Medicine, New Haven, CT, USA.

OBJECTIVE: To assess the effects of oral substitution treatment for opioid-dependent injecting drug users on HIV risk behaviors and infections.

DATA SOURCES: Multiple electronic databases were searched. Reference lists of retrieved articles were checked.

METHODS: Because of varying methodologies of available studies, this systematic review was limited to a descriptive summary, looking at consistency of outcomes across studies.

RESULTS: Twenty-eight studies involving methadone treatment were included in the review. Methadone maintenance treatment is associated with statistically significant reductions in injecting use and sharing of injecting equipment. It is also associated with reductions in numbers of injecting drug users reporting multiple sex partners or exchanges of sex for drugs or money, but has little effect on condom use. It appears that the reductions in risk behaviors do translate into fewer cases of HIV infection.

CONCLUSIONS: Methadone maintenance treatment for injecting drug users significantly reduces the risk of transmission of HIV and should be provided as a component of a strategic approach to the prevention and control of HIV infection. There is insufficient evidence to determine whether other forms of oral substitution treatment also reduce the risk of HIV transmission.

KEY WORDS: HIV infections: prevention and control; substance abuse, intravenous: drug therapy; opioid-related disorders: drug therapy; methadone: therapeutic use.
DOI: 10.1111/j.1525-1497.2005.00287.x
J GEN INTERN MED 2006; 21:193–195.

This paper presents the main findings of a systematic (Cochrane) review. The full review[1] should be consulted for detail of the methods and results.

The goal of this review was to assess the effectiveness of oral substitution treatment for opioid-dependent injecting drug users (IDU) in preventing the spread of HIV.

In the United States, 22% of AIDS cases diagnosed in 2003 were attributed to injection drug use.[2]

Data Sources

Multiple electronic databases were searched from their date of commencement (the latest was 1985) to July 2003 using a strategy addressing opioid dependence, HIV transmission and methadone, and other substitution treatment agents.

Eligible studies included opioid-dependent injecting drug users; involved the oral administration of opioid agonists for substitution treatment; and considered behaviors with a high risk for HIV transmission, or the incidence of HIV infection.

Review Methods

The data from the studies varied in a number of aspects, including the interval between baseline and follow-up interviews; the proportion of participants injecting at baseline; the reporting period for assessment of HIV risk behaviors; and the means of reporting frequency data. This variability reduced the validity of any calculated combined effect. Consequently, this review was limited to a descriptive summary of studies of varying methodologies, which considers the consistency in outcomes reported by the individual studies without metaanalysis to quantify overall effect size.

Primary outcome measures were behaviors with a high risk of transmission of HIV, including injecting drug use, sharing of injecting equipment, unprotected sex, multiple sexual partners, and providing sex in exchange for money or drugs. The incidence of HIV was also assessed.

RESULTS

Description of Included Studies

Twenty-eight studies involving 7,900 participants were included in the review. In all 28 studies, methadone was used for substitution treatment. Only 2 studies[3,4] were randomized controlled trials of oral substitution treatment.

The studies reported 4 types of data: HIV risk behavior at baseline prior to treatment entry, and at follow-up, after a period of methadone treatment (18 studies); HIV risk behavior for participants receiving methadone treatment at the time of assessment compared with participants receiving no or limited methadone treatment (4 studies); HIV risk behaviour in cohorts of drug users either continuing in or ceasing methadone treatment (3 studies); and exposure to methadone treatment for cohorts who HIV seroconverted or remained HIV seronegative over a defined period (4 studies).

The authors have no conflicts of interest to report.

Address correspondence and requests for reprints to Dr. Gowing: Evidence-Based Practice Unit, Drug and Alcohol Services, South Australia, 161 Greenhill Road, Parkside SA 5063, Australia (e-mail: linda.gowing@adelaide.edu.au).

Manuscript received February 16, 2005
Initial editorial decision April 12, 2005
Final acceptance September 2, 2005

Effect of Methadone Treatment on Drug-Related Risk

All 6 studies[3,5–9] that reported data on the proportion of participants reporting injecting use before and after a period of methadone treatment show a significant decrease in injecting from baseline to follow-up.

Similarly 8 studies[3,5,6,10–14] that reported data on the frequency of injecting use all show a significant decrease from baseline to follow-up.

Four studies[12,15,16] that provided data on injecting use for cohorts of drug users receiving or not receiving methadone treatment at the time of a single interview indicate significantly less injecting use for participants in methadone treatment.

All 7 studies[3,5–8,17,18] that reported data on the proportion of participants sharing injecting equipment, before and after a period of methadone treatment showed a reduction. The difference was significant for 6 of the 7 studies. The remaining study[8] reported a nonsignificant reduction (risk ratio [RR] 0.54, 95% confidence interval [CI] 0.23, 1.27).

Four studies provided data on sharing of injecting equipment for participants engaged in methadone treatment compared with those receiving no or limited methadone treatment. In 3 studies[3,16,19] those receiving methadone treatment were significantly less likely to report sharing. In the fourth study,[20] fewer participants in methadone treatment reported sharing injecting equipment, but the difference did not achieve statistical significance (RR 0.79, 95% CI 0.53, 1.19).

Three[6,21,22] of 4 studies that reported rating scale scores of drug-related HIV risk behavior before and after a period of methadone treatment found significant decreases. In the fourth study[4] there was a nonsignificant reduction in the mean score between intake and 6-month follow-up.

Another study[23] reported significantly lower drug risk scores for a cohort of IDU in methadone maintenance with cohorts not in treatment at the time of assessment.

Effect of Methadone Treatment on Sex-Related Risk

In 3[5,6,17] of 4 studies that reported data on the proportion of participants reporting multiple sex partners or exchanges of sex for drugs or money, significantly fewer participants reported these behaviors following methadone treatment, compared with baseline. Relatively few participants in the fourth study[8] reported these behaviors either before (5 of 69) or after (7 of 69) methadone treatment.

Two studies provided data on exchange of sex for drugs or money for cohorts of drug users receiving or not receiving methadone treatment at the time of interview. One study[16] found that significantly fewer of the cohort in methadone treatment reported exchanges; the other study[15] reported a significantly lower frequency of exchanges for the cohort in methadone treatment.

Data on exposure to unprotected sex was reported in different ways. A statistic that could be extracted from most studies was the use of condoms on half or less of occasions. Hence this was used as the definition of exposure to unprotected sex.

Four[5–7,18] of 6 studies reported statistically significant reductions. Of the 2 studies with nonsignificant reductions, 1[17] found that fewer participants reported unprotected sex at follow-up, and in the other[8] most participants reported unprotected sex (84% at baseline, 88% at follow-up).

Two studies[16,19] comparing cohorts of IDU in or out of methadone treatment found no significant difference in condom use. A third study[15] reported a higher frequency of condom use in the 30 days prior to interview for a cohort not in methadone treatment, compared with those currently in methadone treatment (standardized mean difference −0.28, 95% CI −0.55, 0.00).

Two studies[21,22] reported scores of sex-related risk from scales of HIV risk behaviors found a significant reduction in the score from baseline to follow-up after 6 months of substitution treatment. A third study[4] reported a nonstatistically significant reduction.

One study[23] found no difference in sex-related risk scores for IDU currently in methadone maintenance treatment, compared with those previously in, or with no prior history of methadone maintenance.

Effect of Methadone Treatment on Seroconversion

Metzger et al.[16] found that over a period of 18 months, the odds of seroconversion among an untreated group, compared with a group in methadone treatment, were 7.63 (CI 1.99, 29.27, $P<.01$).

Moss et al.[24] reported that 11 of 145 (7.6%) with less than 12 lifetime months in methadone maintenance seroconverted, compared with 11 of 536 (2.1%) with 12 or more lifetime months of methadone maintenance ($P=.002$).

Williams et al.[25] reported a seroconversion rate of 0.7 per 100 person years for those in continuous methadone treatment (mean 29 months), compared with 4.3 per 100 person years for those with interrupted treatment (over a mean 53 months).

Serpelloni et al.[26] found that the risk of HIV infection increased 1.5 times for every 3 months out of methadone treatment in the 12 months prior to seroconversion.

DISCUSSION

The studies identified in this review, whether controlled trials or other types of study, provide evidence that methadone treatment in opioid-dependent IDU is associated with significant reductions in HIV risk behaviors as well as rates of HIV seroconversion.

The studies consistently revealed a decrease in the proportion of participants reporting injecting use, the frequency of injection, the sharing of injecting equipment, and drug-related HIV risk scores.

The data suggest that methadone treatment is associated with a lower likelihood of multiple sex partners or exchanges of sex for drugs or money but no change, or only small decreases, in unprotected sex. This indicates an effect on behaviors that are probably directly related to obtaining drugs, but not on behaviors that are influenced by other factors, such as capacity and willingness to negotiate the use of condoms.

Importantly, the studies of seroconversion rates are consistent in indicating lower rates of seroconversion associated with methadone treatment. This suggests that reductions in risk behavior do translate into actual reductions in cases of HIV infection.

It is unclear to what extent continued injecting behavior during methadone treatment is related to the use of nonopioid drugs. Assessing the extent of reduction of HIV risk behavior associated with methadone treatment of injecting opioid users will require further knowledge of the drugs being injected by those who continue injecting after entry into methadone treatment.

One recent study[27] reported a significant reduction in HIV risk associated with buprenorphine maintenance treatment, but in the absence of other studies, it is currently not possible to compare methadone with other forms of substitution treatment in terms of capacity to reduce HIV risk behavior. Similarly, different types of psychosocial interventions should be compared with methadone treatment on capacity to reduce HIV risk behavior.

Most controlled trials comparing methadone with other substitution pharmacotherapies rely on urine screening and retention in treatment as primary outcome measures. Including an assessment of HIV risk behavior as an outcome measure in controlled trials would add a further important dimension to the assessment of effectiveness of substitution therapies.

The studies identified in this review add to the strong evidence of effectiveness of methadone treatment on drug use, and treatment retention outcomes shown by other systematic reviews while providing important data on the efficacy of methadone treatment in decreasing HIV risk behaviors.[28,29] The provision of methadone treatment for injecting drug users significantly reduces the risk of transmission of HIV and should be provided as a component of a strategic approach to the prevention and control of HIV infection.

Sources of support: Drug and Alcohol Services South Australia; National Addiction Centre, UK; University of Adelaide, SA.

REFERENCES

1. **Gowing L, Farrell M, Bornemann R, Ali R.** Substitution treatment of injecting opioid users for prevention of HIV infection [Cochrane Review]. In: The Cochrane Library, Issue 4. Chichester, UK: John Wiley & Sons; 2004.
2. **Centre for Disease Control and Prevention.** HIV/AIDS Surveillance Report, 2003. Atlanta: U.S. Department of Health and Human Services, 2004. Available from: http://www.cdc.gov/hiv/stats/hasrlink.htm
3. **Dolan KA, Shearer J, MacDonald M, Mattick RP, Hall W, Wodak AD.** A randomised controlled trial of methadone maintenance treatment versus wait list control in an Australian prison system. Drug Alcohol Depend. 2003;72:59–65.
4. **Sees KL, Delucchi KL, Masson C, et al.** Methadone maintenance vs 180-day psychosocially enriched detoxification for treatment of opioid dependence: a randomized controlled trial. JAMA. 2000;283:1303–10.
5. **Camacho LM, Bartholomew NG, Joe GW, Cloud MA, Simpson DD.** Gender, cocaine and during-treatment HIV risk reduction among injection opioid users in methadone maintenance. Drug Alcohol Depend. 1996;41:1–7.
6. **Chatham LR, Hiller ML, Rowan-Szal GA, Joe GW, Simpson DD.** Gender differences at admission and follow-up in a sample of methadone maintenance clients. Subst Use Misuse. 1999;34:1137–65.
7. **Gossop M, Marsden J, Stewart D, Rolfe A.** Patterns of improvement after methadone treatment: 1 year follow-up results from the National Treatment Outcome Research Study (NTORS). Drug Alcohol Depend. 2000;60:275–86.
8. **King VL, Kidorf MS, Stoller KB, Brooner RK.** Influence of psychiatric comorbidity on HIV risk behaviors: changes during drug abuse treatment. J Addict Dis. 2000;19:65–83.
9. **Magura S, Siddiqi Q, Freeman RC, Lipton DS.** Changes in cocaine use after entry to methadone treatment. J Addict Dis. 1991;10:31–45.
10. **Batki SL, Sorensen JL, Gibson DR, Maude-Griffin P.** HIV-infected i.v. drug users in methadone treatment: outcome and psychological correlates—a preliminary report. NIDA Res Monogr. 1989;95:405–6.
11. **Brooner R, Kidorf M, King V, Beilenson P, Svikis D, Vlahov D.** Drug abuse treatment success among needle exchange participants. Public Health Rep. 1998;113:129–39.
12. **Kwiatkowski CF, Booth RE.** Methadone maintenance as HIV risk reduction with street-recruited injecting drug users. J Acquir Immune Defic Syndr. 2001;26:483–9.
13. **Simpson DD, Joe GW, Rowan-Szal G, Greener J.** Client engagement and change during drug abuse treatment. J Subst Abuse. 1995;7:117–34.
14. **Strang J, Marsden J, Cummins M, et al.** Randomized trial of supervised injectable versus oral methadone maintenance: report of feasibility and 6-month outcome. Addiction. 2000;95:1631–45.
15. **Meandzija B, O'Connor PG, Fitzgerald B, Rounsaville BJ, Kosten TR.** HIV infection and cocaine use in methadone maintained and untreated intravenous drug users. Drug Alcohol Depend. 1994;36:109–13.
16. **Metzger DS, Woody GE, McLellan AT, et al.** Human immunodeficiency virus seroconversion among intravenous drug users in- and out-of-treatment: an 18-month prospective follow-up. J Acquir Immune Defic Syndr. 1993;6:1049–56.
17. **Grella CE, Anglin D, Rawson R, Crowley R, Hasson A.** What happens when a demonstration project ends. Consequences for a clinic and its clients. J Subst Abuse Treat. 1996;13:249–56.
18. **Margolin A, Avants SK, Warburton LA, Hawkins KA, Shi J.** A randomized clinical trial of a manual-guided risk reduction intervention for HIV-positive injection drug users. Health Psychol. 2003;22:223–8.
19. **Stark K, Muller R, Bienzle U, Guggenmoos-Holzmann I.** Methadone maintenance treatment and HIV risk-taking behaviour among injecting drug users in Berlin. J Epidemiol Community Health. 1996;50:534–7.
20. **Thiede H, Hagan H, Murrill CS.** Methadone treatment and HIV and hepatitis B and C risk reduction among injectors in the Seattle area. J Urban Health. 2000;77:331–45.
21. **Abbott PJ, Weller SB, Delaney HD, Moore BA.** Community reinforcement approach in the treatment of opiate addicts. Am J Drug Alcohol Abuse. 1998;24:17–30.
22. **Avants SK, Margolin A, Sindelar JL, et al.** Day treatment versus enhanced standard methadone services for opioid-dependent patients: a comparison of clinical efficacy and cost. Am J Psychiatry. 1999;156:27–33.
23. **Baker A, Kochan N, Dixon J, Wodak A, Heather N.** HIV risk-taking behaviour among injecting drug users currently, previously and never enrolled in methadone treatment. Addiction. 1995;90:545–54.
24. **Moss AR, Vranizan K, Gorter R, Bacchetti P, Watters J, Osmond D.** HIV seroconversion in intravenous drug users in San Francisco, 1985–1990. AIDS. 1994;8:223–31.
25. **Williams AB, McNelly EA, Williams AE, D'Aquila RT.** Methadone maintenance treatment and HIV type 1 seroconversion among injecting drug users. AIDS Care. 1992;4:35–41.
26. **Serpelloni G, Carrieri MP, Rezza G, Morganti S, Gomma M, Binkin N.** Methadone treatment as a determinant of HIV risk reduction among injecting drug users: a nested case-control study. AIDS Care. 1994;6:215–20.
27. **Marsch LA, Bickel WK, Badger GJ, Jacobs EA.** Buprenorphine treatment for opioid dependence: the relative efficacy of daily, twice and thrice weekly dosing. Drug Alcohol Depend. 2005;77:195–204.
28. **Mattick RP, Breen C, Kimber J, Davoli M.** Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. Cochrane Library; 2002.
29. **Mattick RP, Kimber J, Breen C, Davoli M.** Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database Syst Rev. 2003;CD002207.